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(54) Title: COMPOUNDS FOR IMMUNOTHERAPY AND DIAGNOSIS OF COLON CANCER AND METHODS FOR THEIR USE					
(57) Abstract					
<p>Compositions and methods for the therapy and diagnosis of cancer, such as colon cancer, are disclosed. Compositions may comprise one or more colon tumor proteins, immunogenic portions thereof, or polynucleotides that encode such portions. Alternatively, a therapeutic composition may comprise an antigen presenting cell that expresses a colon tumor protein, or a T cell that is specific for cells expressing such a protein. Such compositions may be used, for example, for the prevention and treatment of diseases such as colon cancer. Diagnostic methods based on detecting a colon tumor protein, or mRNA encoding such a protein, in a sample are also provided.</p>					

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COMPOUNDS FOR IMMUNOTHERAPY AND DIAGNOSIS
OF COLON CANCER AND METHODS FOR THEIR USE

TECHNICAL FIELD

5 The present invention relates generally to therapy and diagnosis of cancer, such as colon cancer. The invention is more specifically related to polypeptides comprising at least a portion of a colon tumor protein, and to polynucleotides encoding such polypeptides. Such polypeptides and polynucleotides may be used in vaccines and pharmaceutical compositions for prevention and treatment of colon cancer, and for the
10 diagnosis and monitoring of such cancers.

BACKGROUND OF THE INVENTION

Cancer is a significant health problem throughout the world. Although advances have been made in detection and therapy of cancer, no vaccine or other universally successful method for prevention or treatment is currently available. Current therapies, which
15 are generally based on a combination of chemotherapy or surgery and radiation, continue to prove inadequate in many patients.

Colon cancer is the second most frequently diagnosed malignancy in the United States as well as the second most common cause of cancer death. An estimated 95,600 new cases of colon cancer will be diagnosed in 1998, with an estimated 47,700 deaths.
20 The five-year survival rate for patients with colorectal cancer detected in an early localized stage is 92%; unfortunately, only 37% of colorectal cancer is diagnosed at this stage. The survival rate drops to 64% if the cancer is allowed to spread to adjacent organs or lymph nodes, and to 7% in patients with distant metastases.

The prognosis of colon cancer is directly related to the degree of penetration of
25 the tumor through the bowel wall and the presence or absence of nodal involvement, consequently, early detection and treatment are especially important. Currently, diagnosis is aided by the use of screening assays for fecal occult blood, sigmoidoscopy, colonoscopy and double contrast barium enemas. Treatment regimens are determined by the type and stage of the cancer, and include surgery, radiation therapy and/or chemotherapy. Recurrence
30 following surgery (the most common form of therapy) is a major problem and is often the

ultimate cause of death. In spite of considerable research into therapies for the disease, colon cancer remains difficult to diagnose and treat. In spite of considerable research into therapies for these and other cancers, colon cancer remains difficult to diagnose and treat effectively. Accordingly, there is a need in the art for improved methods for detecting and treating such 5 cancers. The present invention fulfills these needs and further provides other related advantages.

SUMMARY OF THE INVENTION

Briefly stated, the present invention provides compositions and methods for the diagnosis and therapy of cancer, such as colon cancer. In one aspect, the present 10 invention provides polypeptides comprising at least a portion of a colon tumor protein, or a variant thereof. Certain portions and other variants are immunogenic, such that the ability of the variant to react with antigen-specific antisera is not substantially diminished. Within certain embodiments, the polypeptide comprises a sequence that is encoded by a polynucleotide sequence selected from the group consisting of: (a) sequences recited in SEQ 15 ID NO: 1-121, 123-197 and 205-486; (b) variants of a sequence recited in SEQ ID NO: 1-121, 123-197 and 205-486; and (c) complements of a sequence of (a) or (b).

The present invention further provides polynucleotides that encode a polypeptide as described above, or a portion thereof (such as a portion encoding at least 15 amino acid residues of a colon tumor protein), expression vectors comprising such 20 polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical compositions comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier.

Within a related aspect of the present invention, vaccines are provided. Such 25 vaccines comprise a polypeptide or polynucleotide as described above and an immunostimulant.

The present invention further provides pharmaceutical compositions that comprise: (a) an antibody or antigen-binding fragment thereof that specifically binds to a colon tumor protein; and (b) a physiologically acceptable carrier.

Within further aspects, the present invention provides pharmaceutical compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a pharmaceutically acceptable carrier or excipient. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B cells.

5 Within related aspects, vaccines are provided that comprise: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) an immunostimulant.

The present invention further provides, in other aspects, fusion proteins that comprise at least one polypeptide as described above, as well as polynucleotides encoding such fusion proteins.

10 Within related aspects, pharmaceutical compositions comprising a fusion protein, or a polynucleotide encoding a fusion protein, in combination with a physiologically acceptable carrier are provided.

15 Vaccines are further provided, within other aspects, that comprise a fusion protein, or a polynucleotide encoding a fusion protein, in combination with an immunostimulant.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient a pharmaceutical composition or vaccine as recited above.

20 The present invention further provides, within other aspects, methods for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a colon tumor protein, wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the protein from the sample.

25 Within related aspects, methods are provided for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated as described above.

Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a colon tumor protein, comprising contacting T cells with one or more of: (i) a polypeptide as described above; (ii) a polynucleotide encoding such a polypeptide; and/or (iii) an antigen presenting cell that expresses such a polypeptide; under

conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Isolated T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population as described above.

The present invention further provides methods for inhibiting the development of a cancer in a patient, comprising the steps of: (a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with one or more of: (i) a polypeptide comprising at least an immunogenic portion of a colon tumor protein; (ii) a polynucleotide encoding such a polypeptide; and (iii) an antigen-presenting cell that expresses such a polypeptide; and (b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient. Proliferated cells may, but need not, be cloned prior to administration to the patient.

Within further aspects, the present invention provides methods for determining the presence or absence of a cancer in a patient, comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of polypeptide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within preferred embodiments, the binding agent is an antibody, more preferably a monoclonal antibody. The cancer may be colon cancer.

The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps of: (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a)

contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a colon tumor protein; (b) detecting in the sample a level of a polynucleotide, preferably mRNA, that hybridizes to the oligonucleotide; and (c) comparing the level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain embodiments, the amount of mRNA is detected via polymerase chain reaction using, for example, at least one oligonucleotide primer that hybridizes to a polynucleotide encoding a polypeptide as recited above, or a complement of such a polynucleotide. Within other embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that hybridizes to a polynucleotide that encodes a polypeptide as recited above, or a complement of such a polynucleotide.

In related aspects, methods are provided for monitoring the progression of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a colon tumor protein; (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polynucleotide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

Within further aspects, the present invention provides antibodies, such as monoclonal antibodies, that bind to a polypeptide as described above, as well as diagnostic kits comprising such antibodies. Diagnostic kits comprising one or more oligonucleotide probes or primers as described above are also provided.

These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached figures. All references disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

SEQUENCE IDENTIFIERS

SEQ ID NO: 1 is a first determined cDNA sequence for Contig 1, showing homology to Neutrophil Gelatinase Associated Lipocalin.

SEQ ID NO: 2 is the determined cDNA sequence for Contig 2, showing no significant homology to any known genes.

SEQ ID NO: 3 is the determined cDNA sequence for Contig 4, showing homology to Carcinoembryonic antigen.

5 SEQ ID NO: 4 is the determined cDNA sequence for Contig 5, showing homology to Carcinoembryonic antigen.

SEQ ID NO: 5 is the determined cDNA sequence for Contig 9, showing homology to Carcinoembryonic antigen.

10 SEQ ID NO: 6 is the determined cDNA sequence for Contig 52, showing homology to Carcinoembryonic antigen.

SEQ ID NO: 7 is the determined cDNA sequence for Contig 6, showing homology to Villin.

SEQ ID NO: 8 is the determined cDNA sequence for Contig 8, showing no significant homology to any known genes.

15 SEQ ID NO: 9 is the determined cDNA sequence for Contig 10, showing homology to Transforming Growth Factor (BIGH3).

SEQ ID NO: 10 is the determined cDNA sequence for Contig 19, showing homology to Transforming Growth Factor (BIGH3).

20 SEQ ID NO: 11 is the determined cDNA sequence for Contig 21, showing homology to Transforming Growth Factor (BIGH3).

SEQ ID NO: 12 is the determined cDNA sequence for Contig 11, showing homology to CO-029.

25 SEQ ID NO: 13 is the determined cDNA sequence for Contig 55, showing homology to CO-029.

SEQ ID NO: 14 is the determined cDNA sequence for Contig 12, showing homology to Chromosome 17, clone hRPC.1171_I_10, also referred to as C798P.

SEQ ID NO: 15 is the determined cDNA sequence for Contig 13, showing no significant homology to any known gene.

30 SEQ ID NO: 16 is the determined cDNA sequence for Contig 14, also referred to as 14261, showing no significant homology to any known gene.

SEQ ID NO: 17 is the determined cDNA sequence for Contig 15, showing homology to Ets-Related Transcription Factor (ERT).

SEQ ID NO: 18 is the determined cDNA sequence for Contig 16, showing homology to Chromosome 5, PAC clone 228g9 (LBNL H142).

5 SEQ ID NO: 19 is the determined cDNA sequence for Contig 24, showing homology to Chromosome 5, PAC clone 228g9 (LBNL H142).

SEQ ID NO: 20 is the determined cDNA sequence for Contig 17, showing homology to Cytokeratin.

10 SEQ ID NO: 21 is the determined cDNA sequence for Contig 18, showing homology to L1-Cadherin.

SEQ ID NO: 22 is the determined cDNA sequence for Contig 20, showing no significant homology to any known gene.

SEQ ID NO: 23 is the determined cDNA sequence for Contig 22, showing homology to Bumetanide-sensitive Na-K-Cl cotransporter (NKCC1).

15 SEQ ID NO: 24 is the determined cDNA sequence for Contig 23, showing no significant homology to any known gene.

SEQ ID NO: 25 is the determined cDNA sequence for Contig 25, showing homology to Macrophage Inflammatory Protein 3 alpha.

20 SEQ ID NO: 26 is the determined cDNA sequence for Contig 26, showing homology to Laminin.

SEQ ID NO: 27 is the determined cDNA sequence for Contig 48, showing homology to Laminin.

SEQ ID NO: 28 is the determined cDNA sequence for Contig 27, showing homology to Myotubularin (MTM1).

25 SEQ ID NO: 29 is the determined cDNA sequence for Contig 28, showing homology to Chromosome 16 BAC clone CIT987SK-A-363E6.

SEQ ID NO: 30 is the determined cDNA sequence for Contig 29, also referred to as C751P and 14247, showing no significant homology to any known gene, but partial homology to Rat GSK-3 β -interacting protein Axil homolog.

30 SEQ ID NO: 31 is the determined cDNA sequence for Contig 30, showing homology to Zinc Finger Transcription Factor (ZNF207).

SEQ ID NO: 32 is the determined cDNA sequence for Contig 31, showing no significant homology to any known gene, but partial homology to *Mus musculus* GOB-4 homolog.

5 SEQ ID NO: 33 is the determined cDNA sequence for Contig 35, showing no significant homology to any known gene, but partial homology to *Mus musculus* GOB-4 homolog.

SEQ ID NO: 34 is the determined cDNA sequence for Contig 32, showing no significant homology to any known gene.

10 SEQ ID NO: 35 is the determined cDNA sequence for Contig 34, showing homology to Desmoglein 2.

SEQ ID NO: 36 is the determined cDNA sequence for Contig 36, showing no significant homology to any known gene.

SEQ ID NO: 37 is the determined cDNA sequence for Contig 37, showing homology to Putative Transmembrane Protein.

15 SEQ ID NO: 38 is the determined cDNA sequence for Contig 38, also referred to as C796P and 14219, showing no significant homology to any known gene.

SEQ ID NO: 39 is the determined cDNA sequence for Contig 40, showing homology to Nonspecific Cross-reacting Antigen.

20 SEQ ID NO: 40 is the determined cDNA sequence for Contig 41, also referred to as C799P and 14308, showing no significant homology to any known gene.

SEQ ID NO: 41 is the determined cDNA sequence for Contig 42, also referred to as C794P and 14309, showing no significant homology to any known gene.

SEQ ID NO: 42 is the determined cDNA sequence for Contig 43, showing homology to Chromosome 1 specific transcript KIAA0487.

25 SEQ ID NO: 43 is the determined cDNA sequence for Contig 45, showing homology to hMCM2.

SEQ ID NO: 44 is the determined cDNA sequence for Contig 46, showing homology to ETS2.

30 SEQ ID NO: 45 is the determined cDNA sequence for Contig 49, showing homology to Pump-1.

SEQ ID NO: 46 is the determined cDNA sequence for Contig 50, also referred to as C792P and 18323, showing no significant homology to any known gene.

SEQ ID NO: 47 is the determined cDNA sequence for Contig 51, also referred to as C795P and 14317, showing no significant homology to any known gene.

5 SEQ ID NO: 48 is the determined cDNA sequence for 11092, showing no significant homology to any known gene.

SEQ ID NO: 49 is the determined cDNA sequence for 11093, showing no significant homology to any known gene.

10 SEQ ID NO: 50 is the determined cDNA sequence for 11094, showing homology to Human Putative Enterocyte Differentiation Protein.

SEQ ID NO: 51 is the determined cDNA sequence for 11095, showing homology to Human Transcriptional Corepressor hKAP1/TIF1B mRNA.

SEQ ID NO: 52 is the determined cDNA sequence for 11096, showing no significant homology to any known gene.

15 SEQ ID NO: 53 is the determined cDNA sequence for 11097, showing homology to Human Nonspecific Antigen.

SEQ ID NO: 54 is the determined cDNA sequence for 11098, showing no significant homology to any known gene.

20 SEQ ID NO: 55 is the determined cDNA sequence for 11099, showing homology to Human Pancreatic Secretory Inhibitor (PST) mRNA.

SEQ ID NO: 56 is the determined cDNA sequence for 11186, showing homology to Human Pancreatic Secretory Inhibitor (PST) mRNA.

SEQ ID NO: 57 is the determined cDNA sequence for 11101, showing homology to Human Chromosome X.

25 SEQ ID NO: 58 is the determined cDNA sequence for 11102, showing homology to Human Chromosome X.

SEQ ID NO: 59 is the determined cDNA sequence for 11103, showing no significant homology to any known gene.

30 SEQ ID NO: 60 is the determined cDNA sequence for 11174, showing no significant homology to any known gene.

SEQ ID NO: 61 is the determined cDNA sequence for 11104, showing homology to Human mRNA for KIAA0154.

SEQ ID NO: 62 is the determined cDNA sequence for 11105, showing homology to Human Apurinic/Apyrimidinic Endonuclease (hap1)mRNA.

5 SEQ ID NO: 63 is the determined cDNA sequence for 11106, showing homology to Human Chromosome 12p13.

SEQ ID NO: 64 is the determined cDNA sequence for 11107, showing homology to Human 90 kDa Heat Shock Protein.

10 SEQ ID NO: 65 is the determined cDNA sequence for 11108, showing no significant homology to any known gene.

SEQ ID NO: 66 is the determined cDNA sequence for 11112, showing no significant homology to any known gene.

SEQ ID NO: 67 is the determined cDNA sequence for 11115, showing no significant homology to any known gene.

15 SEQ ID NO: 68 is the determined cDNA sequence for 11117, showing no significant homology to any known gene.

SEQ ID NO: 69 is the determined cDNA sequence for 11118, showing no significant homology to any known gene.

20 SEQ ID NO: 70 is the determined cDNA sequence for 11119, showing homology to Human Elongation Factor 1-alpha.

SEQ ID NO: 71 is the determined cDNA sequence for 11121, showing homology to Human Lamin B Receptor (LBR) mRNA.

SEQ ID NO: 72 is the determined cDNA sequence for 11122, showing homology to H. sapiens mRNA for Novel Glucocorticoid.

25 SEQ ID NO: 73 is the determined cDNA sequence for 11123, showing homology to H. sapiens mRNA for snRNP protein B.

SEQ ID NO: 74 is the determined cDNA sequence for 11124, showing homology to Human Cisplatin Resistance Associated Beta-protein.

30 SEQ ID NO: 75 is the determined cDNA sequence for 11127, showing homology to M. musculus Calumenin mRNA.

SEQ ID NO: 76 is the determined cDNA sequence for 11128, showing homology to Human ras-related small GTP binding protein.

SEQ ID NO: 77 is the determined cDNA sequence for 11130, showing homology to Human Cosmid U169d2.

5 SEQ ID NO: 78 is the determined cDNA sequence for 11131, showing homology to H. sapiens mRNA for protein homologous to Elongation 1-g.

SEQ ID NO: 79 is the determined cDNA sequence for 11134, showing no significant homology to any known gene.

10 SEQ ID NO: 80 is the determined cDNA sequence for 11135, showing homology to H. sapiens Nieman-Pick (NPC1) mRNA.

SEQ ID NO: 81 is the determined cDNA sequence for 11137, showing homology to H. sapiens mRNA for Niecin b-chain.

SEQ ID NO: 82 is the determined cDNA sequence for 11138, showing homology to Human Endogenous Retroviral Protease mRNA.

15 SEQ ID NO: 83 is the determined cDNA sequence for 11139, showing homology to H. sapiens mRNA for DMBT1 protein.

SEQ ID NO: 84 is the determined cDNA sequence for 11140, showing homology to H. sapiens ras GTPase activating-like protein.

20 SEQ ID NO: 85 is the determined cDNA sequence for 11143, showing homology to Human Acidic Ribosomal Phosphoprotein PO mRNA.

SEQ ID NO: 86 is the determined cDNA sequence for 11144, showing homology to H. sapiens U21 mRNA.

SEQ ID NO: 87 is the determined cDNA sequence for 11145, showing homology to Human GTP-binding protein.

25 SEQ ID NO: 88 is the determined cDNA sequence for 11148, showing homology to H. sapiens U21 mRNA.

SEQ ID NO: 89 is the determined cDNA sequence for 11151, showing no significant homology to any known gene.

30 SEQ ID NO: 90 is the determined cDNA sequence for 11154, showing no significant homology to any known gene.

SEQ ID NO: 91 is the determined cDNA sequence for 11156, showing homology to H. sapiens Ribosomal Protein L27.

SEQ ID NO: 92 is the determined cDNA sequence for 11157, showing homology to H. sapiens Ribosomal Protein L27.

5 SEQ ID NO: 93 is the determined cDNA sequence for 11158, showing no significant homology to any known gene.

SEQ ID NO: 94 is the determined cDNA sequence for 11162, showing homology to Ag-X antigen.

10 SEQ ID NO: 95 is the determined cDNA sequence for 11164, showing homology to H. sapiens mRNA for Signal Recognition Protein sub14.

SEQ ID NO: 96 is the determined cDNA sequence for 11165, showing homology to Human PAC 204e5/127h14.

SEQ ID NO: 97 is the determined cDNA sequence for 11166, showing homology to Human mRNA for KIAA0108.

15 SEQ ID NO: 98 is the determined cDNA sequence for 11167, showing homology to H. sapiens mRNA for Neutrophil Gelatinase assct. Lipocalin.

SEQ ID NO: 99 is the determined cDNA sequence for 11168, showing no significant homology to any known gene.

20 SEQ ID NO: 100 is the determined cDNA sequence for 11172, showing no significant homology to any known gene.

SEQ ID NO: 101 is the determined cDNA sequence for 11175, showing no significant homology to any known gene.

SEQ ID NO: 102 is the determined cDNA sequence for 11176, showing homology to Human maspin mRNA.

25 SEQ ID NO: 103 is the determined cDNA sequence for 11177, showing homology to Human Carcinoembryonic Antigen.

SEQ ID NO: 104 is the determined cDNA sequence for 11178, showing homology to Human A-Tubulin mRNA.

30 SEQ ID NO: 105 is the determined cDNA sequence for 11179, showing homology to Human mRNA for proton-ATPase-like protein.

SEQ ID NO: 106 is the determined cDNA sequence for 11180, showing homology to Human HepG2 3' region cDNA clone hmd.

SEQ ID NO: 107 is the determined cDNA sequence for 11182, showing homology to Human MHC homologous to Chicken B-Complex Protein.

5 SEQ ID NO: 108 is the determined cDNA sequence for 11183, showing homology to Human High Mobility Group Box (SSRP1) mRNA.

SEQ ID NO: 109 is the determined cDNA sequence for 11184, showing no significant homology to any known gene.

10 SEQ ID NO: 110 is the determined cDNA sequence for 11185, showing no significant homology to any known gene.

SEQ ID NO: 111 is the determined cDNA sequence for 11187, showing no significant homology to any known gene.

SEQ ID NO: 112 is the determined cDNA sequence for 11190, showing homology to Human Replication Protein A 70kDa.

15 SEQ ID NO: 113 is the determined cDNA sequence for Contig 47, also referred to as C797P, showing homology to Human Chromosome X clone bWXD342.

SEQ ID NO: 114 is the determined cDNA sequence for Contig 7, showing homology to Equilibrative Nucleoside Transporter 2 (ent2).

20 SEQ ID NO: 115 is the determined cDNA sequence for 14235.1, also referred to as C791P, showing homology to H. sapiens chromosome 21 derived BAC containing ets-2 gene.

SEQ ID NO: 116 is the determined cDNA sequence for 14287.2, showing no significant homology to any known gene, but some degree of homology to Putative Transmembrane Protein.

25 SEQ ID NO: 117 is the determined cDNA sequence for 14233.1, also referred to as Contig 48, showing no significant homology to any known gene.

SEQ ID NO: 118 is the determined cDNA sequence for 14298.2, also referred to as C793P, showing no significant homology to any known gene.

30 SEQ ID NO: 119 is the determined cDNA sequence for 14372, also referred to as Contig 44, showing no significant homology to any known gene.

SEQ ID NO: 120 is the determined cDNA sequence for 14295, showing homology to secreted cement gland protein XAG-2 homolog.

SEQ ID NO: 121 is the determined full-length cDNA sequence for a clone showing homology to Beta IG-H3.

5 SEQ ID NO: 122 is the predicted amino acid sequence for the clone of SEQ ID NO: 121.

SEQ ID NO: 123 is a longer determined cDNA sequence for C751P.

SEQ ID NO: 124 is a longer determined cDNA sequence for C791P.

SEQ ID NO: 125 is a longer determined cDNA sequence for C792P.

10 SEQ ID NO: 126 is a longer determined cDNA sequence for C793P.

SEQ ID NO: 127 is a longer determined cDNA sequence for C794P.

SEQ ID NO: 128 is a longer determined cDNA sequence for C795P.

SEQ ID NO: 129 is a longer determined cDNA sequence for C796P.

SEQ ID NO: 130 is a longer determined cDNA sequence for C797P.

15 SEQ ID NO: 131 is a longer determined cDNA sequence for C798P.

SEQ ID NO: 132 is a longer determined cDNA sequence for C799P.

SEQ ID NO: 133 is a first partial determined cDNA sequence for CoSub-3 (also known as 23569).

20 SEQ ID NO: 134 is a second partial determined cDNA sequence for CoSub-3 (also known as 23569).

SEQ ID NO: 135 is a first partial determined cDNA sequence for CoSub-13 (also known as 23579).

SEQ ID NO: 136 is a second partial determined cDNA sequence for CoSub-13 (also known as 23579).

25 SEQ ID NO: 137 is the determined cDNA sequence for CoSub-17 (also known as 23583).

SEQ ID NO: 138 is the determined cDNA sequence for CoSub-19 (also known as 23585).

30 SEQ ID NO: 139 is the determined cDNA sequence for CoSub-22 (also known as 23714).

SEQ ID NO: 140 is the determined cDNA sequence for CoSub-23 (also known as 23715).

SEQ ID NO: 141 is the determined cDNA sequence for CoSub-26 (also known as 23717).

5 SEQ ID NO: 142 is the determined cDNA sequence for CoSub-33 (also known as 23724).

SEQ ID NO: 143 is the determined cDNA sequence for CoSub-34 (also known as 23725).

10 SEQ ID NO: 144 is the determined cDNA sequence for CoSub-35 (also known as 23726).

SEQ ID NO: 145 is the determined cDNA sequence for CoSub-37 (also known as 23728).

SEQ ID NO: 146 is the determined cDNA sequence for CoSub-39 (also known as 23730).

15 SEQ ID NO: 147 is the determined cDNA sequence for CoSub-42 (also known as 23766).

SEQ ID NO: 148 is the determined cDNA sequence for CoSub-44 (also known as 23768).

20 SEQ ID NO: 149 is the determined cDNA sequence for CoSub-47 (also known as 23771).

SEQ ID NO: 150 is the determined cDNA sequence for CoSub-54 (also known as 23778).

SEQ ID NO: 151 is the determined cDNA sequence for CoSub-55 (also known as 23779).

25 SEQ ID NO: 152 is the determined cDNA sequence for CT1 (also known as 24099).

SEQ ID NO: 153 is the determined cDNA sequence for CT2 (also known as 24100).

SEQ ID NO: 154 is the determined cDNA sequence for CT3 (also known as 24101).

SEQ ID NO: 155 is the determined cDNA sequence for CT6 (also known as 24104).

SEQ ID NO: 156 is the determined cDNA sequence for CT7 (also known as 24105).

30 SEQ ID NO: 157 is the determined cDNA sequence for CT12 (also known as 24110).

SEQ ID NO: 158 is the determined cDNA sequence for CT13 (also known as 24111).

- SEQ ID NO: 159 is the determined cDNA sequence for CT14 (also known as 24112).
- SEQ ID NO: 160 is the determined cDNA sequence for CT15 (also known as 24113).
- SEQ ID NO: 161 is the determined cDNA sequence for CT17 (also known as 24115).
- SEQ ID NO: 162 is the determined cDNA sequence for CT18 (also known as 24116).
- 5 SEQ ID NO: 163 is the determined cDNA sequence for CT22 (also known as 23848).
- SEQ ID NO: 164 is the determined cDNA sequence for CT24 (also known as 23849).
- SEQ ID NO: 165 is the determined cDNA sequence for CT31 (also known as 23854).
- SEQ ID NO: 166 is the determined cDNA sequence for CT34 (also known as 23856).
- SEQ ID NO: 167 is the determined cDNA sequence for CT37 (also known as 23859).
- 10 SEQ ID NO: 168 is the determined cDNA sequence for CT39 (also known as 23860).
- SEQ ID NO: 169 is the determined cDNA sequence for CT40 (also known as 23861).
- SEQ ID NO: 170 is the determined cDNA sequence for CT51 (also known as 24130).
- SEQ ID NO: 171 is the determined cDNA sequence for CT53 (also known as 24132).
- 15 SEQ ID NO: 172 is the determined cDNA sequence for CT63 (also known as 24595).
- SEQ ID NO: 173 is the determined cDNA sequence for CT88 (also known as 24608).
- SEQ ID NO: 174 is the determined cDNA sequence for CT92 (also known as 24800).
- SEQ ID NO: 175 is the determined cDNA sequence for CT94 (also known as 24802).
- SEQ ID NO: 176 is the determined cDNA sequence for CT102 (also known as 24805).
- 20 SEQ ID NO: 177 is the determined cDNA sequence for CT103 (also known as 24806).
- SEQ ID NO: 178 is the determined cDNA sequence for CT111 (also known as 25520).
- SEQ ID NO: 179 is the determined cDNA sequence for CT118 (also known as 25522).
- 25 SEQ ID NO: 180 is the determined cDNA sequence for CT121 (also known as 25523).
- SEQ ID NO: 181 is the determined cDNA sequence for CT126 (also known as 25527).
- 30 SEQ ID NO: 182 is the determined cDNA sequence for CT135 (also known as 25534).

SEQ ID NO: 183 is the determined cDNA sequence for CT140 (also known as 25537).

SEQ ID NO: 184 is the determined cDNA sequence for CT145 (also known as 25542).

5 SEQ ID NO: 185 is the determined cDNA sequence for CT147 (also known as 25543).

SEQ ID NO: 186 is the determined cDNA sequence for CT148 (also known as 25544).

10 SEQ ID NO: 187 is the determined cDNA sequence for CT502 (also known as 26420).

SEQ ID NO: 188 is the determined cDNA sequence for CT507 (also known as 26425).

SEQ ID NO: 189 is the determined cDNA sequence for CT521 (also known as 27366).

15 SEQ ID NO: 190 is the determined cDNA sequence for CT544 (also known as 27375).

SEQ ID NO: 191 is the determined cDNA sequence for CT577 (also known as 27385).

20 SEQ ID NO: 192 is the determined cDNA sequence for CT580 (also known as 27387).

SEQ ID NO: 193 is the determined cDNA sequence for CT594 (also known as 27540).

SEQ ID NO: 194 is the determined cDNA sequence for CT606 (also known as 27547).

25 SEQ ID NO: 195 is the determined cDNA sequence for CT607 (also known as 27548).

SEQ ID NO: 196 is the determined cDNA sequence for CT599 (also known as 27903).

30 SEQ ID NO: 197 is the determined cDNA sequence for CT632 (also known as 27922).

SEQ ID NO: 198 is the predicted amino acid sequence for CT502 (SEQ ID NO: 187).

SEQ ID NO: 199 is the predicted amino acid sequence for CT507 (SEQ ID NO: 188).
SEQ ID NO: 200 is the predicted amino acid sequence for CT521 (SEQ ID NO: 189).
SEQ ID NO: 201 is the predicted amino acid sequence for CT544 (SEQ ID NO: 190).
SEQ ID NO: 202 is the predicted amino acid sequence for CT606 (SEQ ID NO: 194).
5 SEQ ID NO: 203 is the predicted amino acid sequence for CT607 (SEQ ID NO: 195).
SEQ ID NO: 204 is the predicted amino acid sequence for CT632 (SEQ ID NO: 197).
SEQ ID NO: 205 is the determined cDNA sequence for clone 25244.
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SEQ ID NO: 207 is the determined cDNA sequence for clone 25246.
10 SEQ ID NO: 208 is the determined cDNA sequence for clone 25248.
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SEQ ID NO: 210 is the determined cDNA sequence for clone 25250.
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SEQ ID NO: 212 is the determined cDNA sequence for clone 25252.
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20 SEQ ID NO: 218 is the determined cDNA sequence for clone 25259.
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25 SEQ ID NO: 223 is the determined cDNA sequence for clone 25264.
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20 SEQ ID NO: 249 is the determined cDNA sequence for clone 25292.
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25 SEQ ID NO: 254 is the determined cDNA sequence for clone 25297.
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30 SEQ ID NO: 259 is the determined cDNA sequence for clone 25422.
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SEQ ID NO: 261 is the determined cDNA sequence for clone 25424.
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10 SEQ ID NO: 270 is the determined cDNA sequence for clone 25434.
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15 SEQ ID NO: 275 is the determined cDNA sequence for clone 25439.
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5 SEQ ID NO: 296 is the determined cDNA sequence for clone 25856.

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10 SEQ ID NO: 301 is the determined cDNA sequence for clone 25861.

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SEQ ID NO: 303 is the determined cDNA sequence for clone 25863.

SEQ ID NO: 304 is the determined cDNA sequence for clone 25864.

SEQ ID NO: 305 is the determined cDNA sequence for clone 25865.

15 SEQ ID NO: 306 is the determined cDNA sequence for clone 25866.

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SEQ ID NO: 308 is the determined cDNA sequence for clone 25868.

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20 SEQ ID NO: 311 is the determined cDNA sequence for clone 25871.

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SEQ ID NO: 313 is the determined cDNA sequence for clone 25873.

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25 SEQ ID NO: 316 is the determined cDNA sequence for clone 25877.

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SEQ ID NO: 320 is the determined cDNA sequence for clone 25881.

30 SEQ ID NO: 321 is the determined cDNA sequence for clone 25882.

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SEQ ID NO: 323 is the determined cDNA sequence for clone 25884.

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SEQ ID NO: 325 is the determined cDNA sequence for clone 25886.

SEQ ID NO: 326 is the determined cDNA sequence for clone 25887.

5 SEQ ID NO: 327 is the determined cDNA sequence for clone 25888.

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SEQ ID NO: 330 is the determined cDNA sequence for clone 25892.

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10 SEQ ID NO: 332 is the determined cDNA sequence for clone 25895.

SEQ ID NO: 333 is the determined cDNA sequence for clone 25896.

SEQ ID NO: 334 is the determined cDNA sequence for clone 25897.

SEQ ID NO: 335 is the determined cDNA sequence for clone 25899.

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15 SEQ ID NO: 337 is the determined cDNA sequence for clone 25901.

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20 SEQ ID NO: 342 is the determined cDNA sequence for clone 25907.

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SEQ ID NO: 346 is the determined cDNA sequence for clone 25911.

25 SEQ ID NO: 347 is the determined cDNA sequence for clone 25912.

SEQ ID NO: 348 is the determined cDNA sequence for clone 25913.

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30 SEQ ID NO: 352 is the determined cDNA sequence for clone 25917.

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10 SEQ ID NO: 363 is the determined cDNA sequence for clone 25929.
SEQ ID NO: 364 is the determined cDNA sequence for clone 25930.
SEQ ID NO: 365 is the determined cDNA sequence for clone 25931.
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5 SEQ ID NO: 389 is the determined cDNA sequence for clone 31973.

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10 SEQ ID NO: 394 is the determined cDNA sequence for clone 31986.

SEQ ID NO: 395 is the determined cDNA sequence for clone 31954.

SEQ ID NO: 396 is the determined cDNA sequence for clone 31987.

SEQ ID NO: 397 is the determined cDNA sequence for clone 32029.

SEQ ID NO: 398 is the determined cDNA sequence for clone 32028.

15 SEQ ID NO: 399 is the determined cDNA sequence for clone 32012.

SEQ ID NO: 400 is the determined cDNA sequence for clone 31959.

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20 SEQ ID NO: 404 is the determined cDNA sequence for clone 32011.

SEQ ID NO: 405 is the determined cDNA sequence for clone 32022.

SEQ ID NO: 406 is the determined cDNA sequence for clone 32014.

SEQ ID NO: 407 is the determined cDNA sequence for clone 31963.

SEQ ID NO: 408 is the determined cDNA sequence for clone 31989.

25 SEQ ID NO: 409 is the determined cDNA sequence for clone 32015.

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30 SEQ ID NO: 414 is the determined cDNA sequence for clone 32007.

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5 SEQ ID NO: 420 is the determined cDNA sequence for clone 31971.
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10 SEQ ID NO: 425 is the determined cDNA sequence for clone 32006.
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20 SEQ ID NO: 435 is the determined cDNA sequence for clone 32010.
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25 SEQ ID NO: 440 is the determined cDNA sequence for clone 31947.
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30 SEQ ID NO: 445 is the determined cDNA sequence for clone 32024.
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5 SEQ ID NO: 451 is the determined cDNA sequence for clone 32019.
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10 SEQ ID NO: 456 is the determined cDNA sequence for clone 31951.
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SEQ ID NO: 458 is the determined cDNA sequence for clone 31962.
SEQ ID NO: 459 is the determined cDNA sequence for clone 32001.
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SEQ ID NO: 465 is the determined cDNA sequence for clone 31841.
20 SEQ ID NO: 466 is the determined cDNA sequence for clone 31847.
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25 SEQ ID NO: 471 is the determined cDNA sequence for clone 31861.
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30 SEQ ID NO: 476 is the determined cDNA sequence for clone 31877.
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SEQ ID NO: 481 is the determined cDNA sequence for clone 31893.
5 SEQ ID NO: 482 is the determined cDNA sequence for clone 31898.
SEQ ID NO: 483 is the determined cDNA sequence for clone 31901.
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SEQ ID NO: 485 is the determined cDNA sequence for clone 31910.
SEQ ID NO: 486 is the determined cDNA sequence for clone 31914.

10

DETAILED DESCRIPTION OF THE INVENTION

As noted above, the present invention is generally directed to compositions and methods for the therapy and diagnosis of cancer, such as colon cancer. The compositions described herein may include colon tumor polypeptides, polynucleotides encoding such 15 polypeptides, binding agents such as antibodies, antigen presenting cells (APCs) and/or immune system cells (*e.g.*, T cells). Polypeptides of the present invention generally comprise at least a portion (such as an immunogenic portion) of a colon tumor protein or a variant thereof. A "colon tumor protein" is a protein that is expressed in colon tumor cells at a level that is at least two fold, and preferably at least five fold, greater than the level of expression in 20 a normal tissue, as determined using a representative assay provided herein. Certain colon tumor proteins are tumor proteins that react detectably (within an immunoassay, such as an ELISA or Western blot) with antisera of a patient afflicted with colon cancer. Polynucleotides of the subject invention generally comprise a DNA or RNA sequence that encodes all or a portion of such a polypeptide, or that is complementary to such a sequence. 25 Antibodies are generally immune system proteins, or antigen-binding fragments thereof, that are capable of binding to a polypeptide as described above. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B-cells that express a polypeptide as described above. T cells that may be employed within such compositions are generally T cells that are specific for a polypeptide as described above.

The present invention is based on the discovery of human colon tumor proteins. Sequences of polynucleotides encoding specific tumor proteins are provided in SEQ ID NO: 1-121, 123-197 and 205-486.

5 COLON TUMOR PROTEIN POLYNUCLEOTIDES

Any polynucleotide that encodes a colon tumor protein or a portion or other variant thereof as described herein is encompassed by the present invention. Preferred polynucleotides comprise at least 15 consecutive nucleotides, preferably at least 30 consecutive nucleotides and more preferably at least 45 consecutive nucleotides, that encode a portion of a colon tumor protein. More preferably, a polynucleotide encodes an immunogenic portion of a colon tumor protein. Polynucleotides complementary to any such sequences are also encompassed by the present invention. Polynucleotides may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the present invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

Polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a colon tumor protein or a portion thereof) or may comprise a variant of such a sequence. Polynucleotide variants may contain one or more substitutions, additions, deletions and/or insertions such that the immunogenicity of the encoded polypeptide is not diminished, relative to a native tumor protein. The effect on the immunogenicity of the encoded polypeptide may generally be assessed as described herein. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native colon tumor protein or a portion thereof.

Two polynucleotide or polypeptide sequences are said to be "identical" if the sequence of nucleotides or amino acids in the two sequences is the same when aligned for maximum correspondence as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and

compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

5 Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) *Atlas of Protein Sequence and Structure*, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenies pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. 10 (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad. Sci. USA* 80:726-730.

20 Preferably, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide or polypeptide sequence in the comparison window may comprise additions or deletions (i.e. gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequence (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is 25 calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (i.e. the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

30 Variants may also, or alternatively, be substantially homologous to a native gene, or a portion or complement thereof. Such polynucleotide variants are capable of

hybridizing under moderately stringent conditions to a naturally occurring DNA sequence encoding a native colon tumor protein (or a complementary sequence). Suitable moderately stringent conditions include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5 X SSC, overnight; followed by washing twice at 65°C
5 for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS.

It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to the nucleotide sequence of any native gene. Nonetheless, polynucleotides that vary due to
10 differences in codon usage are specifically contemplated by the present invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles
15 may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Polynucleotides may be prepared using any of a variety of techniques. For example, a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (*i.e.*, expression that is at least two fold greater in a colon tumor than in normal tissue, as determined using a representative assay
20 provided herein). Such screens may be performed using a Synteni microarray (Palo Alto, CA) according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Alternatively, polypeptides may be amplified from cDNA
25 prepared from cells expressing the proteins described herein, such as colon tumor cells. Such polynucleotides may be amplified via polymerase chain reaction (PCR). For this approach, sequence-specific primers may be designed based on the sequences provided herein, and may be purchased or synthesized.

An amplified portion may be used to isolate a full length gene from a suitable library (*e.g.*, a colon tumor cDNA library) using well known techniques. Within such
30 techniques, a library (cDNA or genomic) is screened using one or more polynucleotide

probes or primers suitable for amplification. Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be preferred for identifying 5' and upstream regions of genes. Genomic libraries are preferred for obtaining introns and extending 5' sequences.

5 For hybridization techniques, a partial sequence may be labeled (e.g., by nick-translation or end-labeling with ^{32}P) using well known techniques. A bacterial or bacteriophage library is then screened by hybridizing filters containing denatured bacterial colonies (or lawns containing phage plaques) with the labeled probe (*see* Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring
10 Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may be analyzed to determine the amount of additional sequence by, for example, PCR using a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify
15 one or more overlapping clones. The complete sequence may then be determined using standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences are then assembled into a single contiguous sequence. A full length cDNA molecule can be generated by ligating suitable fragments, using well known techniques.

20 Alternatively, there are numerous amplification techniques for obtaining a full length coding sequence from a partial cDNA sequence. Within such techniques, amplification is generally performed via PCR. Any of a variety of commercially available kits may be used to perform the amplification step. Primers may be designed using, for example, software well known in the art. Primers are preferably 22-30 nucleotides in length, have a GC content of at least 50% and anneal to the target sequence at temperatures of about
25 68°C to 72°C. The amplified region may be sequenced as described above, and overlapping sequences assembled into a contiguous sequence.

30 One such amplification technique is inverse PCR (*see* Triglia et al., *Nucl. Acids Res.* 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by

amplification with a primer to a linker sequence and a primer specific to a known region. The amplified sequences are typically subjected to a second round of amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the 5 known sequence, is described in WO 96/38591. Another such technique is known as "rapid amplification of cDNA ends" or RACE. This technique involves the use of an internal primer and an external primer, which hybridizes to a polyA region or vector sequence, to identify sequences that are 5' and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom et al., *PCR Methods Applic.* 1:111-19, 1991) and walking PCR (Parker et al., 10 *Nucl. Acids Res.* 19:3055-60, 1991). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using 15 well known programs (e.g., NCBI BLAST searches), and such ESTs may be used to generate a contiguous full length sequence.

Certain nucleic acid sequences of cDNA molecules encoding portions of colon tumor proteins are provided in SEQ ID NO: 1-121, 123-197 and 205-486. These polynucleotides were isolated from colon tumor cDNA libraries using conventional and/or 20 PCR-based subtraction techniques, as described below.

Polynucleotide variants may generally be prepared by any method known in the art, including chemical synthesis by, for example, solid phase phosphoramidite chemical synthesis. Modifications in a polynucleotide sequence may also be introduced using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis (see 25 Adelman et al., *DNA* 2:183, 1983). Alternatively, RNA molecules may be generated by *in vitro* or *in vivo* transcription of DNA sequences encoding a colon tumor protein, or portion thereof, provided that the DNA is incorporated into a vector with a suitable RNA polymerase promoter (such as T7 or SP6). Certain portions may be used to prepare an encoded polypeptide, as described herein. In addition, or alternatively, a portion may be administered 30 to a patient such that the encoded polypeptide is generated *in vivo* (e.g., by transfecting

antigen-presenting cells, such as dendritic cells, with a cDNA construct encoding a colon tumor polypeptide, and administering the transfected cells to the patient).

A portion of a sequence complementary to a coding sequence (*i.e.*, an antisense polynucleotide) may also be used as a probe or to modulate gene expression. cDNA constructs that can be transcribed into antisense RNA may also be introduced into cells of tissues to facilitate the production of antisense RNA. An antisense polynucleotide may be used, as described herein, to inhibit expression of a tumor protein. Antisense technology can be used to control gene expression through triple-helix formation, which compromises the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors or regulatory molecules (*see* Gee et al., *In Huber and Carr, Molecular and Immunologic Approaches*, Futura Publishing Co. (Mt. Kisco, NY; 1994)). Alternatively, an antisense molecule may be designed to hybridize with a control region of a gene (*e.g.*, promoter, enhancer or transcription initiation site), and block transcription of the gene; or to block translation by inhibiting binding of a transcript to ribosomes.

A portion of a coding sequence, or of a complementary sequence, may also be designed as a probe or primer to detect gene expression. Probes may be labeled with a variety of reporter groups, such as radionuclides and enzymes, and are preferably at least 10 nucleotides in length, more preferably at least 20 nucleotides in length and still more preferably at least 30 nucleotides in length. Primers, as noted above, are preferably 22-30 nucleotides in length.

Any polynucleotide may be further modified to increase stability *in vivo*. Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3' ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiester linkages in the backbone; and/or the inclusion of nontraditional bases such as inosine, queosine and wybutosine, as well as acetyl-, methyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

Nucleotide sequences as described herein may be joined to a variety of other nucleotide sequences using established recombinant DNA techniques. For example, a polynucleotide may be cloned into any of a variety of cloning vectors, including plasmids, phagemids, lambda phage derivatives and cosmids. Vectors of particular interest include expression vectors, replication vectors, probe generation vectors and sequencing vectors. In

general, a vector will contain an origin of replication functional in at least one organism, convenient restriction endonuclease sites and one or more selectable markers. Other elements will depend upon the desired use, and will be apparent to those of ordinary skill in the art.

Within certain embodiments, polynucleotides may be formulated so as to permit entry into a cell of a mammal, and expression therein. Such formulations are particularly useful for therapeutic purposes, as described below. Those of ordinary skill in the art will appreciate that there are many ways to achieve expression of a polynucleotide in a target cell, and any suitable method may be employed. For example, a polynucleotide may be incorporated into a viral vector such as, but not limited to, adenovirus, adeno-associated virus, retrovirus, or vaccinia or other pox virus (*e.g.*, avian pox virus). Techniques for incorporating DNA into such vectors are well known to those of ordinary skill in the art. A retroviral vector may additionally transfer or incorporate a gene for a selectable marker (to aid in the identification or selection of transduced cells) and/or a targeting moiety, such as a gene that encodes a ligand for a receptor on a specific target cell, to render the vector target specific. Targeting may also be accomplished using an antibody, by methods known to those of ordinary skill in the art.

Other formulations for therapeutic purposes include colloidal dispersion systems, such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes. A preferred colloidal system for use as a delivery vehicle *in vitro* and *in vivo* is a liposome (*i.e.*, an artificial membrane vesicle). The preparation and use of such systems is well known in the art.

COLON TUMOR POLYPEPTIDES

Within the context of the present invention, polypeptides may comprise at least an immunogenic portion of a colon tumor protein or a variant thereof, as described herein. As noted above, a "colon tumor protein" is a protein that is expressed by colon tumor cells. Proteins that are colon tumor proteins also react detectably within an immunoassay (such as an ELISA) with antisera from a patient with colon cancer. Polypeptides as described herein may be of any length. Additional sequences derived from the native protein and/or

heterologous sequences may be present, and such sequences may (but need not) possess further immunogenic or antigenic properties.

An "immunogenic portion," as used herein is a portion of a protein that is recognized (*i.e.*, specifically bound) by a B-cell and/or T-cell surface antigen receptor. Such immunogenic portions generally comprise at least 5 amino acid residues, more preferably at least 10, and still more preferably at least 20 amino acid residues of a colon tumor protein or a variant thereof. Certain preferred immunogenic portions include peptides in which an N-terminal leader sequence and/or transmembrane domain have been deleted. Other preferred immunogenic portions may contain a small N- and/or C-terminal deletion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids), relative to the mature protein.

Immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, *Fundamental Immunology*, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with antigen-specific antibodies, antisera and/or T-cell lines or clones. As used herein, antisera and antibodies are "antigen-specific" if they specifically bind to an antigen (*i.e.*, they react with the protein in an ELISA or other immunoassay, and do not react detectably with unrelated proteins). Such antisera and antibodies may be prepared as described herein, and using well known techniques. An immunogenic portion of a native colon tumor protein is a portion that reacts with such antisera and/or T-cells at a level that is not substantially less than the reactivity of the full length polypeptide (*e.g.*, in an ELISA and/or T-cell reactivity assay). Such immunogenic portions may react within such assays at a level that is similar to or greater than the reactivity of the full length polypeptide. Such screens may generally be performed using methods well known to those of ordinary skill in the art, such as those described in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. For example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the sera to the immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, ¹²⁵I-labeled Protein A.

As noted above, a composition may comprise a variant of a native colon tumor protein. A polypeptide "variant," as used herein, is a polypeptide that differs from a native colon tumor protein in one or more substitutions, deletions, additions and/or insertions, such

that the immunogenicity of the polypeptide is not substantially diminished. In other words, the ability of a variant to react with antigen-specific antisera may be enhanced or unchanged, relative to the native protein, or may be diminished by less than 50%, and preferably less than 20%, relative to the native protein. Such variants may generally be identified by modifying 5 one of the above polypeptide sequences and evaluating the reactivity of the modified polypeptide with antigen-specific antibodies or antisera as described herein. Preferred variants include those in which one or more portions, such as an N-terminal leader sequence or transmembrane domain, have been removed. Other preferred variants include variants in which a small portion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids) has been removed 10 from the N- and/or C-terminal of the mature protein.

Polypeptide variants preferably exhibit at least about 70%, more preferably at least about 90% and most preferably at least about 95% identity (determined as described above) to the identified polypeptides.

Preferably, a variant contains conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydropathic nature of the polypeptide to be substantially unchanged. Amino acid substitutions may generally be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For 15 example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, 20 gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain non-conservative changes. In a preferred embodiment, variant polypeptides differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino acids that have 25 minimal influence on the immunogenicity, secondary structure and hydropathic nature of the polypeptide.

As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (e.g., poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

Polypeptides may be prepared using any of a variety of well known techniques. Recombinant polypeptides encoded by DNA sequences as described above may be readily prepared from the DNA sequences using any of a variety of expression vectors known to those of ordinary skill in the art. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a DNA molecule that encodes a recombinant polypeptide. Suitable host cells include prokaryotes, yeast and higher eukaryotic cells. Preferably, the host cells employed are *E. coli*, yeast or a mammalian cell line such as COS or CHO. Supernatants from suitable host/vector systems which secrete recombinant protein or polypeptide into culture media may be first concentrated using a commercially available filter. Following concentration, the concentrate may be applied to a suitable purification matrix such as an affinity matrix or an ion exchange resin. Finally, one or more reverse phase HPLC steps can be employed to further purify a recombinant polypeptide.

Portions and other variants having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may also be generated by synthetic means, using techniques well known to those of ordinary skill in the art. For example, such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. See Merrifield, *J. Am. Chem. Soc.* 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems Division (Foster City, CA), and may be operated according to the manufacturer's instructions.

Within certain specific embodiments, a polypeptide may be a fusion protein that comprises multiple polypeptides as described herein, or that comprises at least one polypeptide as described herein and an unrelated sequence, such as a known tumor protein. A

fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner), preferably T helper epitopes recognized by humans, or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing 5 fusion partners. Other fusion partners may be selected so as to increase the solubility of the protein or to enable the protein to be targeted to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the protein.

Fusion proteins may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion protein is expressed as a recombinant 10 protein, allowing the production of increased levels, relative to a non-fused protein, in an expression system. Briefly, DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that 15 the reading frames of the sequences are in phase. This permits translation into a single fusion protein that retains the biological activity of both component polypeptides.

A peptide linker sequence may be employed to separate the first and the second polypeptide components by a distance sufficient to ensure that each polypeptide folds 20 into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into the fusion protein using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact 25 with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which 30 may be usefully employed as linkers include those disclosed in Maratea et al., *Gene* 40:39-46, 1985; Murphy et al., *Proc. Natl. Acad. Sci. USA* 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and

second polypeptides have non-essential N-terminal amino acid regions that can be used to separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of 5 DNA are located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

Fusion proteins are also provided that comprise a polypeptide of the present invention together with an unrelated immunogenic protein. Preferably the immunogenic 10 protein is capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (see, for example, Stoute et al. *New Engl. J. Med.*, 336:86-91, 1997).

Within preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium *Haemophilus influenza B* 15 (WO 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (e.g., the first N-terminal 100-110 amino acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in *E. coli* (thus functioning as 20 an expression enhancer). The lipid tail ensures optimal presentation of the antigen to antigen presenting cells. Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemagglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

In another embodiment, the immunological fusion partner is the protein known 25 as LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is derived from *Streptococcus pneumoniae*, which synthesizes an N-acetyl-L-alanine amidase known as amidase LYTA (encoded by the LytA gene; *Gene* 43:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible for the affinity to the choline or to some choline 30 analogues such as DEAE. This property has been exploited for the development of *E. coli* C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid

proteins containing the C-LYTA fragment at the amino terminus has been described (*see Biotechnology* 10:795-798, 1992). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion protein. A repeat portion is found in the C-terminal region starting at residue 178. A particularly preferred repeat portion incorporates residues 188-305.

In general, polypeptides (including fusion proteins) and polynucleotides as described herein are isolated. An "isolated" polypeptide or polynucleotide is one that is removed from its original environment. For example, a naturally-occurring protein is isolated if it is separated from some or all of the coexisting materials in the natural system. Preferably, such polypeptides are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99% pure. A polynucleotide is considered to be isolated if, for example, it is cloned into a vector that is not a part of the natural environment.

BINDING AGENTS

The present invention further provides agents, such as antibodies and antigen-binding fragments thereof, that specifically bind to a colon tumor protein. As used herein, an antibody, or antigen-binding fragment thereof, is said to "specifically bind" to a colon tumor protein if it reacts at a detectable level (within, for example, an ELISA) with a colon tumor protein, and does not react detectably with unrelated proteins under similar conditions. As used herein, "binding" refers to a noncovalent association between two separate molecules such that a complex is formed. The ability to bind may be evaluated by, for example, determining a binding constant for the formation of the complex. The binding constant is the value obtained when the concentration of the complex is divided by the product of the component concentrations. In general, two compounds are said to "bind," in the context of the present invention, when the binding constant for complex formation exceeds about 10^3 L/mol. The binding constant may be determined using methods well known in the art.

Binding agents may be further capable of differentiating between patients with and without a cancer, such as colon cancer, using the representative assays provided herein. In other words, antibodies or other binding agents that bind to a colon tumor protein will generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, and will generate a negative signal indicating the absence of the disease in at least about 90% of individuals without the cancer. To determine whether a binding agent satisfies

this requirement, biological samples (*e.g.*, blood, sera, sputum, urine and/or tumor biopsies) from patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. It will be apparent that a statistically significant number of samples with and without the disease should be assayed. Each binding agent should satisfy the above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. *See, e.g.,* Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (*e.g.*, mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically. Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol.* 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (*i.e.*, reactivity with the polypeptide of interest). Such cell lines may be produced, for example,

from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are selected and their culture supernatants tested for binding activity against the polypeptide.

10 Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or 15 the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

Within certain embodiments, the use of antigen-binding fragments of 20 antibodies may be preferred. Such fragments include Fab fragments, which may be prepared using standard techniques. Briefly, immunoglobulins may be purified from rabbit serum by affinity chromatography on Protein A bead columns (Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988) and digested by papain to yield Fab and Fc fragments. The Fab and Fc fragments may be separated by affinity 25 chromatography on protein A bead columns.

Monoclonal antibodies of the present invention may be coupled to one or more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include ⁹⁰Y, ¹²³I, ¹²⁵I, ¹³¹I, ¹⁸⁶Re, ¹⁸⁸Re, ²¹¹At, and ²¹²Bi. Preferred drugs include methotrexate, and pyrimidine and 30 purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid.

Preferred toxins include ricin, abrin, diphtheria toxin, cholera toxin, gelonin, *Pseudomonas* exotoxin, *Shigella* toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (*e.g.*, covalently bonded) to a suitable monoclonal antibody either directly or indirectly (*e.g.*, via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (*e.g.*, a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents, which otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl groups, sulfhydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, *e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of different cleavable linker groups have been described. The mechanisms for the intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (*e.g.*, U.S. Patent No. 4,489,710, to Spitzer), by irradiation of a photolabile bond (*e.g.*, U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (*e.g.*, U.S. Patent No. 4,638,045, to Kohn et al.), by serum complement-mediated hydrolysis (*e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (*e.g.*, U.S. Patent No. 4,569,789, to Blattler et al.).

It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody. Regardless of the particular embodiment, immunoconjugates with more than one agent may 5 be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or linkers which provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (e.g., 10 U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (e.g., U.S. Patent No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (e.g., U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include 15 radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

20 A variety of routes of administration for the antibodies and immunoconjugates may be used. Typically, administration will be intravenous, intramuscular, subcutaneous or in the bed of a resected tumor. It will be evident that the precise dose of the antibody/immunoconjugate will vary depending upon the antibody used, the antigen density on the tumor, and the rate of clearance of the antibody.

25

T CELLS

Immunotherapeutic compositions may also, or alternatively, comprise T cells specific for a colon tumor protein. Such cells may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example, T cells may be isolated from bone marrow, 30 peripheral blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the ISOLEX™ system, available from

Nexell Therapeutics Inc., Irvine, CA . Alternatively, T cells may be derived from related or unrelated humans, non-human mammals, cell lines or cultures.

T cells may be stimulated with a colon tumor polypeptide, polynucleotide encoding a colon tumor polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide. Preferably, a colon tumor polypeptide or polynucleotide is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for a colon tumor polypeptide if the T cells kill target cells coated with the polypeptide or expressing a gene encoding the polypeptide. T cell specificity may be evaluated using any of a variety of standard techniques. For example, within a chromium release assay or proliferation assay, a stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et al., *Cancer Res.* 54:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell proliferation can be detected by measuring an increased rate of DNA synthesis (*e.g.*, by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a colon tumor polypeptide (100 ng/ml - 100 µg/ml, preferably 200 ng/ml - 25 µg/ml) for 3 - 7 days should result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (*e.g.*, TNF or IFN- γ) is indicative of T cell activation (*see* Coligan et al., *Current Protocols in Immunology*, vol. 1, Wiley Interscience (Greene 1998)). T cells that have been activated in response to a colon tumor polypeptide, polynucleotide or polypeptide-expressing APC may be CD4 $^{+}$ and/or CD8 $^{+}$. Colon tumor protein-specific T cells may be expanded using standard techniques. Within preferred embodiments, the T cells are derived from either a patient or a related, or unrelated, donor and are administered to the patient following stimulation and expansion.

For therapeutic purposes, CD4 $^{+}$ or CD8 $^{+}$ T cells that proliferate in response to a colon tumor polypeptide, polynucleotide or APC can be expanded in number either *in vitro*

or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a variety of ways. For example, the T cells can be re-exposed to a colon tumor polypeptide, or a short peptide corresponding to an immunogenic portion of such a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize a colon tumor polypeptide. Alternatively, one or more T cells that proliferate in the presence of a colon tumor protein can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

PHARMACEUTICAL COMPOSITIONS AND VACCINES

Within certain aspects, polypeptides, polynucleotides, T cells and/or binding agents disclosed herein may be incorporated into pharmaceutical compositions or immunogenic compositions (*i.e.*, vaccines). Pharmaceutical compositions comprise one or more such compounds and a physiologically acceptable carrier. Vaccines may comprise one or more such compounds and an immunostimulant. An immunostimulant may be any substance that enhances or potentiates an immune response to an exogenous antigen. Examples of immunostimulants include adjuvants, biodegradable microspheres (*e.g.*, polylactic galactide) and liposomes (into which the compound is incorporated; *see e.g.*, Fullerton, U.S. Patent No. 4,235,877). Vaccine preparation is generally described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Pharmaceutical compositions and vaccines within the scope of the present invention may also contain other compounds, which may be biologically active or inactive. For example, one or more immunogenic portions of other tumor antigens may be present, either incorporated into a fusion polypeptide or as a separate compound, within the composition or vaccine.

A pharmaceutical composition or vaccine may contain DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. As noted above, the DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, bacteria and viral expression systems. Numerous gene delivery techniques are well known in the art, such as those described by Rolland, *Crit. Rev. Therap. Drug Carrier Systems* 15:143-198, 1998, and references cited therein. Appropriate nucleic acid expression systems contain the

necessary DNA sequences for expression in the patient (such as a suitable promoter and terminating signal). Bacterial delivery systems involve the administration of a bacterium (such as *Bacillus-Calmette-Guerrin*) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope. In a preferred embodiment, the 5 DNA may be introduced using a viral expression system (e.g., vaccinia or other pox virus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic (defective), replication competent virus. Suitable systems are disclosed, for example, in Fisher-Hoch et al., *Proc. Natl. Acad. Sci. USA* 86:317-321, 1989; Flexner et al., *Ann. N.Y. Acad. Sci.* 569:86-103, 1989; Flexner et al., *Vaccine* 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 10 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805; Berkner, *Biotechniques* 6:616-627, 1988; Rosenfeld et al., *Science* 252:431-434, 1991; Kolls et al., *Proc. Natl. Acad. Sci. USA* 91:215-219, 1994; Kass-Eisler et al., *Proc. Natl. Acad. Sci. USA* 90:11498-11502, 1993; Guzman et al., *Circulation* 88:2838-2848, 1993; and Guzman et al., *Cir. Res.* 73:1202-1207, 1993. 15 Techniques for incorporating DNA into such expression systems are well known to those of ordinary skill in the art. The DNA may also be "naked," as described, for example, in Ulmer et al., *Science* 259:1745-1749, 1993 and reviewed by Cohen, *Science* 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

20 While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration, including for example, topical, oral, nasal, intravenous, intracranial, intraperitoneal, subcutaneous or intramuscular administration. 25 For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a fat, a wax or a buffer. For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (e.g., polylactate polyglycolate) may also be 30 employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268 and

5,075,109.

Such compositions may also comprise buffers (e.g., neutral buffered saline or phosphate buffered saline), carbohydrates (e.g., glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, chelating agents such as EDTA or glutathione, adjuvants (e.g., aluminum hydroxide) and/or preservatives. Alternatively, compositions of the present invention may be formulated as a lyophilizate. Compounds may also be encapsulated within liposomes using well known technology.

Any of a variety of immunostimulants may be employed in the vaccines of this invention. For example, an adjuvant may be included. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, *Bordetella pertussis* or *Mycobacterium tuberculosis* derived proteins. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quill A. Cytokines, such as GM-CSF or interleukin-2, -7, or -12, may also be used as adjuvants.

Within the vaccines provided herein, the adjuvant composition is preferably designed to induce an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (e.g., IFN- γ , TNF α , IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (e.g., IL-4, IL-5, IL-6 and IL-10) tend to favor the induction of humoral immune responses. Following application of a vaccine as provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using standard assays. For a review of the families of cytokines, see Mosmann and Coffman, *Ann. Rev. Immunol.* 7:145-173, 1989.

Preferred adjuvants for use in eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A (3D-MPL), together with an aluminum salt. MPL adjuvants are available from Ribi ImmunoChem Research Inc. (Hamilton, MT) (see US Patent Nos. 5 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555. Another preferred adjuvant is a saponin, preferably QS21, which may be used alone or in combination with other adjuvants. For example, an enhanced system involves the combination of a 10 monophosphoryl lipid A and saponin derivative, such as the combination of QS21 and 3D-MPL as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with cholesterol, as described in WO 96/33739. Other preferred formulations comprises an oil-in-water emulsion and tocopherol. A particularly potent adjuvant formulation involving QS21, 3D-MPL and tocopherol in an oil-in-water emulsion is 15 described in WO 95/17210. Any vaccine provided herein may be prepared using well known methods that result in a combination of antigen, immune response enhancer and a suitable carrier or excipient.

The compositions described herein may be administered as part of a sustained release formulation (*i.e.*, a formulation such as a capsule, sponge or gel (composed of 20 polysaccharides, for example) that effects a slow release of compound following administration). Such formulations may generally be prepared using well known technology and administered by, for example, oral, rectal or subcutaneous implantation, or by implantation at the desired target site. Sustained-release formulations may contain a polypeptide, polynucleotide or antibody dispersed in a carrier matrix and/or contained within 25 a reservoir surrounded by a rate controlling membrane. Carriers for use within such formulations are biocompatible, and may also be biodegradable; preferably the formulation provides a relatively constant level of active component release. The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be 30 treated or prevented.

Any of a variety of delivery vehicles may be employed within pharmaceutical

compositions and vaccines to facilitate production of an antigen-specific immune response that targets tumor cells. Delivery vehicles include antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the antigen, to improve activation and/or maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

10 Certain preferred embodiments of the present invention use dendritic cells or progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature* 392:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (*see* Timmerman and Levy, *Ann. Rev. Med.* 50:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*), their ability to take up, process and present antigens with high efficiency, and their ability to activate naïve T cell responses. Dendritic cells may, of course, be engineered to express specific cell-surface receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex vivo*, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (*see* Zitvogel et al., *Nature Med.* 4:594-600, 1998).

20 Dendritic cells and progenitors may be obtained from peripheral blood, bone marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNF α to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into dendritic cells by adding to the culture medium combinations of 30 GM-CSF, IL-3, TNF α , CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce differentiation, maturation and proliferation of dendritic cells.

Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which correlates with the high expression of Fc γ receptor and mannose receptor. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II MHC, adhesion molecules (*e.g.*, CD54 and CD11) and costimulatory molecules (*e.g.*, CD40, CD80, CD86 and 4-1BB).

APCs may generally be transfected with a polynucleotide encoding a colon tumor protein (or portion or other variant thereof) such that the colon tumor polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place *ex vivo*, and a composition or vaccine comprising such transfected cells may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection that occurs *in vivo*. *In vivo* and *ex vivo* transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., *Immunology and cell Biology* 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells with the colon tumor polypeptide, DNA (naked or within a plasmid vector) or RNA; or with antigen-expressing recombinant bacterium or viruses (*e.g.*, vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that provides T cell help (*e.g.*, a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated immunological partner, separately or in the presence of the polypeptide.

CANCER THERAPY

In further aspects of the present invention, the compositions described herein may be used for immunotherapy of cancer, such as colon cancer. Within such methods, pharmaceutical compositions and vaccines are typically administered to a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human. A patient may or

may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions and vaccines may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. A cancer may be diagnosed using criteria generally accepted in the art, including the presence of a malignant tumor. Pharmaceutical compositions and vaccines may 5 be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host immune system to react against tumors with the administration of immune response-modifying agents (such as 10 polypeptides and polynucleotides disclosed herein).

Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not necessarily depend on an intact host immune system. Examples of effector cells 15 include T cells as discussed above, T lymphocytes (such as CD8⁺ cytotoxic T lymphocytes and CD4⁺ T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors specific for the polypeptides recited herein may be cloned, expressed and 20 transferred into other vectors or effector cells for adoptive immunotherapy. The polypeptides provided herein may also be used to generate antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding 25 single antigen-specific effector cells to several billion in number with retention of antigen recognition *in vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient 30 number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte, fibroblast and/or B cells, may be pulsed with immunoreactive

polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*. Studies have shown that cultured effector cells can be induced to grow *in vivo* and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (see, for example, Cheever et al., *Immunological Reviews* 157:177, 1997).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into antigen presenting cells taken from a patient and clonally propagated *ex vivo* for transplant back into the same patient. Transfected cells may be reintroduced into the patient using any means known in the art, preferably in sterile form by intravenous, intracavitory, intraperitoneal or intratumor administration.

Routes and frequency of administration of the therapeutic compositions disclosed herein, as well as dosage, will vary from individual to individual, and may be readily established using standard techniques. In general, the pharmaceutical compositions and vaccines may be administered by injection (*e.g.*, intracutaneous, intramuscular, intravenous or subcutaneous), intranasally (*e.g.*, by aspiration) or orally. Preferably, between 1 and 10 doses may be administered over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50% above the basal (*i.e.*, untreated) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells *in vitro*. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to non-vaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 25 µg to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient,

but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such a response can be monitored by establishing an improved clinical outcome (e.g., more frequent remissions, complete or partial, or longer disease-free survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to a colon tumor protein generally correlate with an improved clinical outcome. Such immune responses may generally be evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

METHODS FOR DETECTING CANCER

In general, a cancer may be detected in a patient based on the presence of one or more colon tumor proteins and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, sputum, urine and/or tumor biopsies) obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as colon cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the agent in the biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer. In general, a colon tumor sequence should be present at a level that is at least three fold higher in tumor tissue than in normal tissue

There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. See, e.g., Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c) comparing the level of polypeptide with a predetermined cut-off value.

In a preferred embodiment, the assay involves the use of binding agent immobilized on a solid support to bind to and remove the polypeptide from the remainder of

the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G, protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding agent. Suitable polypeptides for use within such assays include full length colon tumor proteins and portions thereof to which the binding agent binds, as described above.

The solid support may be any material known to those of ordinary skill in the art to which the tumor protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about 10 µg, and preferably about 100 ng to about 1 µg, is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (see, e.g., Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

In certain embodiments, the assay is a two-antibody sandwich assay. This assay may be performed by first contacting an antibody that has been immobilized on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20TM (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.*, incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with colon cancer. Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20TM. The second antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

5 The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of time. Unbound detection reagent is then removed and bound detection reagent is detected using the reporter group. The method employed for detecting
10 the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the
15 addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

20 To determine the presence or absence of a cancer, such as colon cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average mean signal obtained when the immobilized antibody is incubated with samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred embodiment, the cut-off value is determined using a Receiver Operator Curve, according to
25 the method of Sackett et al., *Clinical Epidemiology: A Basic Science for Clinical Medicine*, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (*i.e.*, sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (*i.e.*, the value
30 that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered

positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

5 In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent. Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1 μ g, and more preferably from about 50 ng to about 500 ng. Such tests can typically be performed with a very small amount of biological sample.

25 Of course, numerous other assay protocols exist that are suitable for use with the tumor proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to those of ordinary skill in the art that the above protocols may be readily modified to use colon tumor polypeptides to detect antibodies that bind to such polypeptides in a biological sample. The detection of such 30 colon tumor protein specific antibodies may correlate with the presence of a cancer.

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a colon tumor protein in a biological sample. Within certain methods, a biological sample comprising CD4⁺ and/or CD8⁺ T cells isolated from a patient is incubated with a colon tumor polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells. For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may be incubated *in vitro* for 2-9 days (typically 4 days) at 37°C with one or more representative polypeptides (e.g., 5 - 25 µg/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of colon tumor polypeptide to serve as a control. For CD4⁺ T cells, activation is preferably detected by evaluating proliferation of the T cells. For CD8⁺ T cells, activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding a colon tumor protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to amplify a portion of a colon tumor cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (*i.e.*, hybridizes to) a polynucleotide encoding the colon tumor protein. The amplified cDNA is then separated and detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a colon tumor protein may be used in a hybridization assay to detect the presence of polynucleotide encoding the tumor protein in a biological sample.

To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%, preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a colon tumor protein that is at least 10 nucleotides, and preferably at least 20 nucleotides, in length. Preferably, oligonucleotide primers and/or probes will

hybridize to a polynucleotide encoding a polypeptide disclosed herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers comprise at 5 least 10 contiguous nucleotides, more preferably at least 15 contiguous nucleotides, of a DNA molecule having a sequence recited in SEQ ID NO: 1-121, 123-197 and 205-486. Techniques for both PCR based assays and hybridization assays are well known in the art (see, for example, Mullis et al., *Cold Spring Harbor Symp. Quant. Biol.*, 51:263, 1987; Erlich ed., *PCR Technology*, Stockton Press, NY, 1989).

10 One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy tissue, and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on 15 biological samples taken from a test patient and from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered positive.

20 In another embodiment, the disclosed compositions may be used as markers for the progression of cancer. In this embodiment, assays as described above for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) or polynucleotide evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In 25 general, a cancer is progressing in those patients in whom the level of polypeptide or polynucleotide detected increases over time. In contrast, the cancer is not progressing when the level of reactive polypeptide or polynucleotide either remains constant or decreases with time.

30 Certain *in vivo* diagnostic assays may be performed directly on a tumor. One such assay involves contacting tumor cells with a binding agent. The bound binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may

also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

As noted above, to improve sensitivity, multiple colon tumor protein markers may be assayed within a given sample. It will be apparent that binding agents specific for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of tumor protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or alternatively, assays for tumor proteins provided herein may be combined with assays for other known tumor antigens.

10

DIAGNOSTIC KITS

The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For example, one container within a kit may contain a monoclonal antibody or fragment thereof that specifically binds to a colon tumor protein. Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements, such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable for direct or indirect detection of antibody binding.

Alternatively, a kit may be designed to detect the level of mRNA encoding a colon tumor protein in a biological sample. Such kits generally comprise at least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a colon tumor protein. Such an oligonucleotide may be used, for example, within a PCR or hybridization assay. Additional components that may be present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding a colon tumor protein.

The following Examples are offered by way of illustration and not by way of limitation.

EXAMPLES

5

Example 1

ISOLATION AND CHARACTERIZATION OF COLON TUMOR POLYPEPTIDES BY
PCR-BASED SUBTRACTION AND MICROARRAY ANALYSIS

A cDNA library was constructed in the PCR2.1 vector (Invitrogen, Carlsbad, CA) by subtracting a pool of three colon tumors with a pool of normal colon, spleen, brain, liver, kidney, lung, stomach and small intestine using PCR subtraction methodologies (Clontech, Palo Alto, CA). The subtraction was performed using a PCR-based protocol, which was modified to generate larger fragments. Within this protocol, tester and driver double stranded cDNA were separately digested with five restriction enzymes that recognize six-nucleotide restriction sites (MluI, Mscl, PvuII, SalI and StuI). This digestion resulted in an average cDNA size of 600 bp, rather than the average size of 300 bp that results from digestion with RsaI according to the Clontech protocol. This modification did not affect the subtraction efficiency. Two tester populations were then created with different adapters, and the driver library remained without adapters.

The tester and driver libraries were then hybridized using excess driver cDNA. In the first hybridization step, driver was separately hybridized with each of the two tester cDNA populations. This resulted in populations of (a) unhybridized tester cDNAs, (b) tester cDNAs hybridized to other tester cDNAs, (c) tester cDNAs hybridized to driver cDNAs, and (d) unhybridized driver cDNAs. The two separate hybridization reactions were then combined, and rehybridized in the presence of additional denatured driver cDNA. Following this second hybridization, in addition to populations (a) through (d), a fifth population (e) was generated in which tester cDNA with one adapter hybridized to tester cDNA with the second adapter. Accordingly, the second hybridization step resulted in enrichment of differentially expressed sequences which could be used as templates for PCR amplification with adaptor-specific primers.

The ends were then filled in, and PCR amplification was performed using adaptor-specific primers. Only population (e), which contained tester cDNA that did not

hybridize to driver cDNA, was amplified exponentially. A second PCR amplification step was then performed, to reduce background and further enrich differentially expressed sequences.

This PCR-based subtraction technique normalizes differentially expressed 5 cDNAs so that rare transcripts that are over-expressed in colon tumor tissue may be recoverable. Such transcripts would be difficult to recover by traditional subtraction methods.

To characterize the complexity and redundancy of the subtracted library, 96 clones were randomly picked and 65 were sequenced, as previously described. These 10 sequences were further characterized by comparison with the most recent Genbank database (April, 1998) to determine their degree of novelty. No significant homologies were found to 21 of these clones, hereinafter referred to as 11092, 11093, 11096, 11098, 11103, 11174, 11108, 11112, 11115, 11117, 11118, 11134, 11151, 11154, 11158, 11168, 11172, 11175, 11184, 11185 and 11187. The determined cDNA sequences for these clones are provided in 15 SEQ ID NO: 48, 49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101 and 109-111, respectively.

Two-thousand clones from the above mentioned cDNA subtraction library were randomly picked and submitted to a round of PCR amplification. Briefly, 0.5 µl of glycerol stock solution was added to 99.5 µl of pcr MIX (80 µl H₂O, 10 µl 10X PCR Buffer, 6 µl 25 mM MgCl₂, 1 µl 10 mM dNTPs, 1 µl 100 mM M13 forward primer 20 (CACGACGTTGTAAAACGACGG), 1 µl 100 mM M13 reverse primer (CACAGGAAACAGCTATGACC)), and 0.5 µl 5 u/ml Taq polymerase (primers provided by (Operon Technologies, Alameda, CA). The PCR amplification was run for thirty cycles under the following conditions: 95°C for 5 min., 92°C for 30 sec., 57°C for 40 sec., 75°C for 2 min. and 75°C for 5 minutes.

25 mRNA expression levels for representative clones were determined using microarray technology (Synteni, Palo Alto, CA) in colon tumor tissues (n=25), normal colon tissues (n=6), kidney, lung, liver, brain, heart, esophagus, small intestine, stomach, pancreas, adrenal gland, salivary gland, resting PBMC, activated PBMC, bone marrow, dendritic cells, spinal cord, blood vessels, skeletal muscle, skin, breast and fetal tissues. The number of 30 tissue samples tested in each case was one (n=1), except where specifically noted above; additionally, all the above-mentioned tissues were derived from humans. The PCR

amplification products were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, and fluorescent-labeled cDNA probes were generated by reverse transcription according to the protocol provided by Synteni. The microarrays were probed with the labeled 5 cDNA probes, the slides scanned, and fluorescence intensity was measured. This intensity correlates with the hybridization intensity.

One hundred and forty nine clones showed two or more fold over-expression in the colon tumor probe group as compared to the normal tissue probe group. These cDNA clones were further characterized by DNA sequencing with a Perkin Elmer/Applied 10 Biosystems Division Automated Sequencer Model 373A and/or Model 377 (Foster City, CA). These sequences were compared to known sequences in the most recent GenBank database. No significant homologies to human gene sequences were found in forty nine of these clones, represented by the following sixteen cDNA consensus sequences: SEQ ID NO: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46 and 47, hereinafter referred to as Contig 2, 8, 15 13, 14, 20, 23, 29, 31, 35, 32, 36, 38, 41, 42, 50 and 51, respectively). Contig 29 (SEQ ID NO: 30) was found to be a Rat GSK-3- β -interacting protein Axil homolog. Also, Contigs 31 and 35 (SEQ ID NO: 32 and 33, respectively) were found to be a Mus musculus GOB-4 homolog. The determined cDNA sequences of SEQ ID NO: 1, 3-7, 9-14, 17-21, 23, 25-29, 31, 35, 37, 39, 42-45, 50, 51, 53, 55-58, 61-64, 70-78, 80-88, 91, 92, 94-98, 102-108 and 112 20 were found to show some homology to previously identified genes sequences.

Microarray analysis demonstrated Contig 2 (SEQ ID NO: 2) showed over-expression in 34% of colon tumors tested, as well as increased expression in normal pancreatic tissue, with no over-expression in normal colon tissues. Upon further analysis, Contigs 2, 8 and 23 were found to share homology to the known gene GW112. Contigs 4, 5, 25 9 and 52 showed homology to carcinoembryonic antigen (SEQ ID NO: 3, 4, 5 and 6, respectively). A representative sampling of these fragments showed over-expression in 85% of colon tumors, with over-expression in normal bone marrow and 3/6 normal colon tissues. Contig 6 (SEQ ID NO: 7), showing homology to the known gene sequence for villin, and was over-expressed in about half of all colon tumors tested, with a limited degree of low level 30 over-expression in normal colon. Contig 12 (SEQ ID NO: 14), showing homology to Chromosome 17, clone hRPC.1171_I_10, also referred to as C798P, was over-expressed in

approximately 70% of colon tumors tested, with low over-expression in 1/6 normal colon samples. Contig 14, also referred to as 14261 (SEQ ID NO: 16), showing no significant homology to any known gene, showed over-expression in 44% of colon tumors tested, with low level expression in half of normal colon tissues, as well as small intestine and pancreatic tissue. Contig 18 (SEQ ID NO: 21), showing homology to the known gene for L1-cadherin, showed over-expression in approximately half of colon tumors and low level over-expression in 3/6 normal colon tissues tested. Contig 22 (SEQ ID NO: 23), showing homology to Bumetanide-sensitive Na-K-Cl cotransporter was over-expressed in 70% of colon tumors and no over-expression in all normal tissues tested. Contig 25 (SEQ ID NO: 25), showing homology to macrophage inflammatory protein-3 α , was over-expressed in over 40% of colon tumors and in activated PBMC. Contigs 26 and 48 (SEQ ID NOS: 25 and 26), showing homology to the sequence for laminin, was over-expressed in 48% of colon tumors and with low over-expression in stomach tissue. Contig 28 (SEQ ID NO: 29), showing homology to the known gene sequence for Chromosome 16 BAC clone CIT987SK-A-363E6, was over-expressed in 33% of colon tumors tested with normal stomach and 2/6 normal colon tissues showing low level over-expression. Contigs 29, 31 and 35 (SEQ ID NOS: 30, 32 and 33, respectively), also referred to as C751P, an unknown sequence showing limited and partial homology to Rat GSK-3 β -interacting protein Axil homolog and Mus musculus GOB-4 homolog, was over-expressed in 74% of colon tumors and no over-expression in all normal tissues tested. Contig 34 (SEQ ID NO: 35), showing homology to the known sequence for desmoglein 2, was over-expressed in 56% of colon tumors and showed low level over-expression in 1/6 normal colon tissues. Contig 36 (SEQ ID NO: 36), an unknown sequence also referred to as C793P, showed over-expression in 30% of colon tumor tissues tested. Contig 37 and 14287.2 (SEQ ID NOS: 37 and 116), an unknown sequence, but with limited (89%) homology to the known sequence for putative transmembrane protein was over-expressed in 70% of colon tumors, as well as in normal lung tissue and 3/6 normal colon tissues tested. Contig 38, also referred to as C796P and 14219 (SEQ ID NO: 38), showing no significant homology to any known gene, was over-expressed in 38% in colon tumors and no elevated over-expression in any normal tissues. Contig 41 (SEQ ID NO: 40), also referred to as C799P and 14308, an unknown sequence showing no significant homology to any known gene, was over-expressed in 22% of colon tumors. Contig 42, (SEQ ID NO: 41), also

referred to as C794P and 14309, an unknown sequence with no significant homology to any known gene, was over-expressed in 63% of colon tumors tested, as well as in 3/6 normal colon tissues. Contig 43 (SEQ ID NO: 42), showing homology to the known sequence for Chromosome 1 specific transcript KIAA0487 was over-expressed in 85% of colon tumors tested and in normal lung and 4/6 normal colon tissues. Contig 49 (SEQ ID NO: 45), showing homology to the known sequence for pump-1, was over-expressed in 44% of colon tumors and no over-expression in all normal tissues tested. Contig 50 (SEQ ID NO: 46), also referred to as C792P and 18323, showing no significant homology to any known gene, was over-expressed in 33% of colon tumors with no detectable over-expression in any normal tissues tested. Contig 51 (SEQ ID NO: 47), also referred to as C795P and 14317 was over-expressed in 11% of colon tumors.

Additional microarray analysis yielded seven clones showing two or more fold over-expression in the colon tumor probe group as compared to the normal tissue probe group. Three of these clones demonstrated particularly good colon tumor specificity, and are represented by SEQ ID NO: 115, 116 and 120. Specifically, SEQ ID NO: 115, referred to as C791P or 14235, which shows homology to the known gene sequence for *H. sapiens* chromosome 21 derived BAC containing ets-2 gene, was over-expressed in 89% of colon tumors tested and in 5/6 normal colon tissues, as well as over-expressed at low levels in normal lung and activated PBMC. Microarray analysis for SEQ ID NO: 116 is discussed above. SEQ ID NO: 120, referred to as 14295, showing homology to the known gene sequence for secreted cement gland protein XAG-2 homolog, was over-expressed in 70% of colon tumors and in 5/6 normal colon tissues, as well as low level over-expression in normal small intestine, stomach and lung. All clones showing over-expression in colon tumor were sequenced and these sequences compared to the most recent Genbank database (February 12, 1999). Of the seven clones, three contained sequences that did not share significant homology to any known gene sequences, represented by SEQ ID NO: 116, 117 and 119. To the best of the inventors' knowledge, none of these sequences have been previously shown to be present in colon. The determined cDNA sequences of the remaining clones (SEQ ID NO: 113-115 and 120) were found to show some homology to previously identified genes.

Further analysis identified a clone which was recovered several times by PCR subtraction and by expression screening using a mouse anti-scid antiserum. The determined

full length cDNA sequence for this clone is provided in SEQ ID NO: 121, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 122. This clone is homologous with the known gene Beta IG-H3, as disclosed in U.S. Patent No. 5,444,164. Microarray analysis demonstrated this clone to be over-expressed in 75 to 80% of 5 colon tumors tested (n=27), with no over-expression in normal colon samples (n=6), but with some low level over-expression in other normal tissues tested.

Further analysis of the PCR-subtraction library described above led to the isolation of longer cDNA sequences for the clones of SEQ ID NO: 30, 115, 46, 118, 41, 47, 10 38, 113, 14 and 40 (known as C751P, C791P, C792P, C793P, C794P, C795P, C796P, C797P, C798P and C799P, respectively). These determined cDNA sequences are provided in SEQ ID NO: 123-132, respectively.

Using PCR subtraction methodology described above with minor modifications, transcripts from a pool of three moderately differentiated colon adenocarcinoma samples were subtracted with a set of transcripts from normal brain, 15 pancreas, bone marrow, liver, heart, lung, stomach and small intestine. Modifications of the above protocol were included at the cDNA digestion steps and in the tester to drive hybridization ratios. In a first subtraction, the restriction enzymes PvuII, DraI, MscI and StuI were used to digest cDNAs, and the tester to driver ratio was 1:40, as suggested by Clontech. In a second subtraction, DraI, MscI and StuI were used for cDNA digestion and a tester to 20 driver ratio of 1:76 was used. Following the PCR amplification steps, the cDNAs were cloned into pCR2.1 plasmid vector. The determined cDNA sequences of 167 isolated clones are provided in SEQ ID NO: 205-371. These sequences were compared to sequences in the public databases as described above. The sequences of SEQ ID NO: 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 25 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369 and 371 were found to show some homology to previously identified ESTs. The remaining sequences were found to show some homology to previously identified genes.

Using the PCR subtraction technology described above, a cDNA library from 30 a pool of primary colon tumors was subtracted with a cDNA library prepared from normal tissues, including brain, bone marrow, kidney, heart, lung, liver, pancreas, small intestine,

stomach and trachea. The determined cDNA sequences for 90 clones isolated in this subtraction are provided in SEQ ID NO: 372-461. Comparison of these sequences with those in the public databases as described above, revealed no homologies to the sequences of SEQ ID NO: 426, 445 and 453. The sequences of SEQ ID NO: 372-378, 380-404, 406, 409-417, 5 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455 and 457-461 showed some homology to previously identified genes, while the sequences of SEQ ID NO: 379, 405, 407, 408, 418, 424, 430-432, 437, 442, 444, 452 and 456 showed some homology to previously isolated ESTs.

10

Example 2

ISOLATION OF TUMOR POLYPEPTIDES USING SCID-PASSAGED TUMOR RNA

Human colon tumor antigens were obtained using SCID mouse passaged 15 colon tumor RNA as follows. Human colon tumor was implanted in SCID mice and harvested, as described in Patent Application Serial No. 08/556,659 filed 11/13/95, U.S. Patent No. 5,986,170 . First strand cDNA was synthesized from poly A+ RNA from three SCID mouse-passaged colon tumors using a Lambda ZAP Express cDNA synthesis kit (Stratagene). The reactions were pooled and digested with RNase A, T1 and H to cleave the 20 RNA and then treated with NaOH to degrade the RNA. The resulting cDNA was annealed with biotinylated (Vector Labs, Inc., Burlingame, CA) cDNA from a normal resting PBMC plasmid library (constructed from Superscript plasmid System, Gibco BRL), and subtracted with streptavidin by phenol/chloroform extraction. Second strand cDNA was synthesized 25 from the subtracted first strand cDNA and digested with S1 nuclease (Gibco BRL). The cDNA was blunted with Pfu polymerase and EcoRI adaptors (Stratagene) were ligated to the ends. The cDNA was phosphorylated with T4 polynucleotide kinase, digested with restriction endonuclease XhoI, and size selected with Sephadryl S-400 (Sigma). Fractions were pooled, ligated to Lambda ZAP Express arms (Stratagene) and packaged with Gigapack Gold III extract (Stratagene). Random plaques were picked, phagemid was excised, 30 transformed into XLOR cells (Stratagene) and resulting plasmid DNA (Qiagen Inc., Valencia, CA) was sequenced as described above. The determined cDNA sequences for 17

clones isolated as described above are provided in SEQ ID NO: 133-151, wherein 133 and 134 represent partial sequences of a clone referred to as CoSub-3 and SEQ ID NO: 135 and 136 represent partial sequences of a clone referred to as CoSub-13. These sequences were compared with those in the public databases as described above. The sequences of SEQ ID NO: 139 and 149 showed no significant homologies to any previously identified sequences. The sequences of SEQ ID NO: 138, 140, 141, 142, 143, 148 and 149 showed some homology to previously isolated expressed sequence tags (ESTs). The sequences of SEQ ID NO: 133-137, 144-147, 150 and 151 showed some homology to previously isolated gene sequences.

10

Example 3

USE OF MOUSE ANTISERA TO IDENTIFY DNA SEQUENCES ENCODING COLON TUMOR ANTIGENS

This example illustrates the isolation of cDNA sequences encoding colon tumor antigens by screening of colon tumor cDNA libraries with mouse anti-tumor sera.

A cDNA expression library was prepared from SCID mouse-passaged human colon tumor poly A+ RNA using a Stratagene (La Jolla, CA) Lambda ZAP Express kit, following the manufacturer's instructions. Sera was obtained from the colon tumor-bearing SCID mouse. This serum was injected into normal mice to produce anti-colon tumor serum. Approximately 600,000 PFUs were screened from the unamplified library using this antiserum. Using a goat anti-mouse IgG-A-M (H+L) alkaline phosphatase second antibody developed with NBT/BCIP (BRL Labs.), positive plaques were identified. Phage was purified and phagemid excised for several clones with inserts in a pBK-CMV vector for expression in prokaryotic or eukaryotic cells.

The determined cDNA sequences for 46 of the isolated clones are provided in SEQ ID NO: 152-197. The predicted amino acid sequences for the cDNA sequences of SEQ ID NO: 187, 188, 189, 190, 194, 195 and 197 are provided in SEQ ID NO: 198-204, respectively. The determined cDNA sequences were compared with those in the public database as described above. The sequences of SEQ ID NO: 156, 168, 184, 189, 192 and 196 showed some homology to previously isolated ESTs. The sequences of SEQ ID NO: 152-

155, 157-167, 169-182, 183, 185-188, 190, 194, 195 and 197 showed some homology to previously identified genes.

Example 4

5 ISOLATION AND CHARACTERIZATION OF COLON TUMOR
POLYPEPTIDES BY CONVENTIONAL SUBTRACTION

Two cDNA libraries were constructed and used to create a subtracted cDNA library as follows.

10 Using the GibcoBRL Superscript Plasmid System with minor modifications, two cDNA libraries were created. The first library, referred to as CTCL, was prepared from a pool of mRNA samples from three colon adenocarcinoma tissue samples. Two of the samples were described as Duke's stage C and one as Duke's stage B. All three samples were grade III in histological status. A second library (referred to as DriverLibpcDNA3.1+) 15 was prepared from a pool of normal tissues, namely liver, pancreas, skin, bone marrow, resting PBMC, stomach and brain. Both libraries were prepared using the manufacturer's instructions with the following modifications: an EcoRI-NotI 5' cDNA adapter was used instead of the provided reagent; the vector pCDNA3.1(+) (Invitrogen) was substituted for the pSPORT vector; and the ligated DNA molecules were transformed into ElectroMaxDH10B 20 electrocompetent cells. Clones from the libraries were analyzed by restriction digest and sequencing to determine average insert size, quality of the library and complexity of the library. DNA was prepared from each library and digested.

The driver DNA was biotinylated and hybridized with the colon library tester DNA at a ratio of 10:1. After two rounds of hybridizations, streptavidin incubations and 25 extractions, the remaining colon cDNAs were size-selected by column chromatography and cloned into the pCMV-Script vector from Stratagene. Clones from this subtracted library (referred to as CTCL-S1) were characterized as described above for the unsubtracted libraries.

30 The determined cDNA sequences for 18 clones isolated from the CTCL-S1 library are provided in SEQ ID NO: 462-479. Comparison of these sequences with those in the public databases, as described above, revealed no significant homologies to the sequences

of SEQ ID NO: 476, 477 and 479. The remaining sequences showed some homology to previously identified genes.

In further studies, a cDNA library was prepared from a pool of mRNA from three metastatic colon adenocarcinomas derived from liver tissue samples. All samples were 5 described as Duke's stage D. Conventional subtraction was performed as described above, using the DriverLibpcDNA3.1+ library described above as the driver. The resulting subtracted library (referred to as CMCL-S1) was characterized by isolating a set of clones for restriction analysis and sequencing.

The determined cDNA sequences for 7 clones isolated from the CMCL-S1 10 library are provided in SEQ ID NO: 480-486. Comparison of these sequences with those in the public databases revealed no significant homologies to the sequence of SEQ ID NO: 483. The sequences of SEQ ID NO: 480-482 and 484-486 were found to show some homology to previously identified genes.

15

Example 5

SYNTHESIS OF POLYPEPTIDES

Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems Division 430A peptide synthesizer using FMOC chemistry with HPTU (O-Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence 20 may be attached to the amino terminus of the peptide to provide a method of conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from the solid support may be carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the 25 peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be dissolved in water containing 0.1% trifluoroacetic acid (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of 0%-60% acetonitrile (containing 0.1% TFA) in water (containing 0.1% TFA) may be used to elute the peptides. Following lyophilization of the pure fractions, the peptides may be characterized using electrospray or 30 other types of mass spectrometry and by amino acid analysis.

From the foregoing it will be appreciated that, although specific embodiments of the invention have been described herein for purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the invention is not limited except as by the appended claims.

CLAIMS

1. An isolated polypeptide comprising at least an immunogenic portion of a colon tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

- (a) sequences recited in SEQ ID NO: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479 and 483;
- (b) sequences that hybridize to a sequence of SEQ ID NO: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479 and 483 under moderately stringent conditions; and
- (c) a complement of a sequence of (a) or (b).

2. An isolated polypeptide according to claim 1, wherein the polypeptide comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168,

170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234,
236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273,
279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345,
347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429,
5 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479 and 483 or a complement
of any of the foregoing polynucleotide sequences.

3. An isolated polypeptide comprising a sequence recited in any one of
SEQ ID NO: 122 and 198-204.

10 4. An isolated polynucleotide encoding at least 15 amino acid residues of
a colon tumor protein, or a variant thereof that differs in one or more substitutions, deletions,
additions and/or insertions such that the ability of the variant to react with antigen-specific
antisera is not substantially diminished, wherein the tumor protein comprises an amino acid
sequence that is encoded by a polynucleotide comprising a sequence recited in any one of
15 SEQ ID NO: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79,
89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182,
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20 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436,
438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479 and 483 or a complement of any of
the foregoing sequences.

25 5. An isolated polynucleotide encoding a colon tumor protein, or a variant
thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a
polynucleotide comprising a sequence recited in any one of SEQ ID NO: 2, 8, 15, 16, 22, 24,
30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-
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310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479 and 483 or a complement of any of the foregoing sequences.

5 6. An isolated polynucleotide comprising a sequence recited in any one of SEQ ID NO: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 10 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479 and 483.

15 7. An isolated polynucleotide comprising a sequence that hybridizes to a sequence recited in any one of SEQ ID NO: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479 and 483 under moderately stringent conditions.

20 8. An isolated polynucleotide complementary to a polynucleotide according to any one of claims 4-7.

25 9. An expression vector comprising a polynucleotide according to any one of claims 4-8.

30 10. A host cell transformed or transfected with an expression vector according to claim 9.

11. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a colon tumor protein that comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 2, 8, 15, 16, 22, 24, 5 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116- 119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 10 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479 and 483 or a complement of any of the foregoing polynucleotide sequences.

12. A fusion protein comprising at least one polypeptide according to 15 claim 1.

13. A fusion protein according to claim 12, wherein the fusion protein comprises an expression enhancer that increases expression of the fusion protein in a host cell transfected with a polynucleotide encoding the fusion protein.

20 14. A fusion protein according to claim 12, wherein the fusion protein comprises a T helper epitope that is not present within the polypeptide of claim 1.

25 15. A fusion protein according to claim 12, wherein the fusion protein comprises an affinity tag.

16. An isolated polynucleotide encoding a fusion protein according to claim 12.

30 17. A pharmaceutical composition comprising a physiologically acceptable carrier and at least one component selected from the group consisting of:

- (a) a polypeptide according to claim 1;
- (b) a polynucleotide according to claim 4;
- (c) an antibody according to claim 11;
- (d) a fusion protein according to claim 12; and
- (e) a polynucleotide according to claim 16.

5

18. A vaccine comprising an immunostimulant and at least one component selected from the group consisting of:

- (a) a polypeptide according to claim 1;
- (b) a polynucleotide according to claim 4;
- (c) an antibody according to claim 11;
- (d) a fusion protein according to claim 12; and
- (e) a polynucleotide according to claim 16.

10

15

19. A vaccine according to claim 18, wherein the immunostimulant is an adjuvant.

20. A vaccine according to any claim 18, wherein the immunostimulant induces a predominantly Type I response.

20

21. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a pharmaceutical composition according to claim 17.

25

22. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a vaccine according to claim 20.

30

23. A pharmaceutical composition comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with a pharmaceutically acceptable carrier or excipient.

24. A pharmaceutical composition according to claim 23, wherein the antigen presenting cell is a dendritic cell or a macrophage.

25. A vaccine comprising an antigen-presenting cell that expresses a 5 polypeptide according to claim 1, in combination with an immunostimulant.

26. A vaccine according to claim 25, wherein the immunostimulant is an adjuvant.

10 27. A vaccine according to claim 25, wherein the immunostimulant induces a predominantly Type I response.

28. A vaccine according to claim 25, wherein the antigen-presenting cell is a dendritic cell.

15 29. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of an antigen-presenting cell that expresses a polypeptide encoded by a polynucleotide recited in any one of SEQ ID NO: 1-121, 123-197 and 205-486, and thereby inhibiting the development of a cancer in the patient.

20 30. A method according to claim 29, wherein the antigen-presenting cell is a dendritic cell.

25 31. A method according to any one of claims 21, 22 and 29, wherein the cancer is colon cancer.

32. A method for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a colon tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded 30 by a polynucleotide sequence selected from the group consisting of:

(i) polynucleotides recited in any one of SEQ ID NO: 1-121, 123-

197 and 205-486; and

(ii) complements of the foregoing polynucleotides;

wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the antigen from the sample.

5

33. A method according to claim 32, wherein the biological sample is blood or a fraction thereof.

34. A method for inhibiting the development of a cancer in a patient,
10 comprising administering to a patient a biological sample treated according to the method of
claim 50.

35. A method for stimulating and/or expanding T cells specific for a colon tumor protein, comprising contacting T cells with at least one component selected from the
15 group consisting of:

- (i) a polypeptide according to claim 1;
- (ii) a polypeptide encoded by a polynucleotide comprising a sequence provided in any one of SEQ ID NO: 1-121, 123-197 and 205-486;
- (iii) a polynucleotide encoding a polypeptide of (i) or (ii); and
- (iv) an antigen presenting cell that expresses a polypeptide of (i) or (ii),
20 under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.

36. An isolated T cell population, comprising T cells prepared according to
25 the method of claim 35.

37. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population according to
claim 36.

30

38. A method for inhibiting the development of a cancer in a patient,

comprising the steps of:

- (a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with at least one component selected from the group consisting of:
- (i) a polypeptide according to claim 1;
 - 5 (ii) a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NO: 1-121, 123-197 and 205-486;
 - (iii) a polynucleotide encoding a polypeptide of (i) or (ii); and
 - (iv) an antigen-presenting cell that expresses a polypeptide of (i) or
- 10 (ii);

such that T cells proliferate; and

- (b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient.

15 39. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

- (a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with at least one component selected from the group consisting of:
- (i) a polypeptide according to claim 1;
 - 20 (ii) a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NO: 1-121, 123-197 and 205-486;
 - (iii) a polynucleotide encoding a polypeptide of (i) or (ii); and
 - (iii) an antigen-presenting cell that expresses a polypeptide of (i) or

25 (ii);

such that T cells proliferate;

- (b) cloning at least one proliferated cell to provide cloned T cells; and
- (c) administering to the patient an effective amount of the cloned T cells, and thereby inhibiting the development of a cancer in the patient.

30

40. A method for determining the presence or absence of a cancer in a

patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient with a binding agent that binds to a colon tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

5 (i) polynucleotides recited in any one of SEQ ID NO: 1-121, 123-197 and 205-486; and

(ii) complements of the foregoing polynucleotides;

(b) detecting in the sample an amount of polypeptide that binds to the binding agent; and

10 (c) comparing the amount of polypeptide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

41. A method according to claim 40, wherein the binding agent is an antibody.

15 42. A method according to claim 43, wherein the antibody is a monoclonal antibody.

43. A method according to claim 40, wherein the cancer is colon cancer.

20 44. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a colon tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-121, 123-197 and 205-486 or a complement of any of the foregoing polynucleotides;

(b) detecting in the sample an amount of polypeptide that binds to the binding agent;

30 (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and

(d) comparing the amount of polypeptide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

45. A method according to claim 44, wherein the binding agent is an antibody.

46. A method according to claim 45, wherein the antibody is a monoclonal antibody.

10 47. A method according to claim 44, wherein the cancer is a colon cancer.

48. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

15 (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a colon tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-121, 123-197 and 205-486 or a complement of any of the foregoing polynucleotides;

20 (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and

(c) comparing the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

25 49. A method according to claim 48, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

50. A method according to claim 48, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

30 51. A method for monitoring the progression of a cancer in a patient,

comprising the steps of:

(a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a colon tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a

5 polynucleotide sequence recited in any one of SEQ ID NO: 1-121, 123-197 and 205-486 or a complement of any of the foregoing polynucleotides;

(b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide;

(c) repeating steps (a) and (b) using a biological sample obtained from the
10 patient at a subsequent point in time; and

(d) comparing the amount of polynucleotide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

15 52. A method according to claim 51, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

53. A method according to claim 51, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

20 54. A diagnostic kit, comprising:

(a) one or more antibodies according to claim 11; and
(b) a detection reagent comprising a reporter group.

25 55. A kit according to claim 54, wherein the antibodies are immobilized on a solid support.

56. A kit according to claim 54, wherein the detection reagent comprises an anti-immunoglobulin, protein G, protein A or lectin.

30 57. A kit according to claim 54, wherein the reporter group is selected

from the group consisting of radioisotopes, fluorescent groups, luminescent groups, enzymes, biotin and dye particles.

5 58. An oligonucleotide comprising 10 to 40 contiguous nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes a colon tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479 and 483 or a complement of any of the foregoing polynucleotides.

15

15 59. A oligonucleotide according to claim 58, wherein the oligonucleotide comprises 10-40 contiguous nucleotides recited in any one of SEQ ID NO: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479 and 483.

25

25 60. A diagnostic kit, comprising:
 (a) an oligonucleotide according to claim 59; and
 (b) a diagnostic reagent for use in a polymerase chain reaction or hybridization assay.

SEQUENCE LISTING

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<120> COMPOUNDS FOR IMMUNOTHERAPY AND
DIAGNOSIS OF COLON CANCER AND METHODS FOR THEIR USE

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<210> 11						
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<221> misc_feature						
<222> (1) ... (411)						
<223> n = A,T,C or G						
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<213> Homo sapien	
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<210> 15	
<211> 688	
<212> DNA	
<213> Homo sapien	
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<222> (1)...(688)	
<223> n = A,T,C or G	
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caaaagcacata gaagcacatc acatacacca gcaaggtttc caactactgc actgattaac	180
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ttctgagctg ccttggaaag gaagttatga ggtagaagat tctactgact ttttagtaagg	600
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<210> 16	
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<213> Homo sapien

<400> 16

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agaataaccc tgatcttac ttaaaggagt tgctaaatct tgctgaaaac aataaaggga	240
aagttgtggc aataggagaa tgcggacttg atttgaccc gactgcagtt ttgtcccaa	300
gatactcaac tcaaataattt taaaaaacag tttgaactgt cagaacaaac aaaattacca	360
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<210> 17

<211> 407

<212> DNA

<213> Homo sapien

<400> 17

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ccagtggcgt gatgctggga cccttaggat ggggctccca gtcctttct cctgtgaatg	300
gaggcagaag acctccaata aagtgccttc tgggctttttt ctaacctttt tcttagctac	360
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<210> 18

<211> 405

<212> DNA

<213> Homo sapien

<400> 18

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caagttgttt ggacagaaag gctacagagt gtggctctgg ctcttgtta agaattacga	180
ccacgctaac catgcctagg aaggaaagga gttattttt tggaaaagg tgctggggtt	240
tgagagatca gtcggacacg attggcaggg agagcacgtg tggtttatg agaattatgc	300
ccgagatagg taacagatga ggaagaaattt tgggcttgat tgaagtaatg gggctgtct	360
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<210> 19

<211> 401

<212> DNA

<213> Homo sapien

<400> 19

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gctgctcaa gcgggattag gggcggcgtg ggagcctaga gtggagaga ttaagctgaa	180
gggaggtctt gtggtaaggg gtatgtatcat gggatgtta gaagaaacat ttgtcgtata	240
gaatgattgg tggatggctgt gatacggtt tggatgatt gagaagctaa atggaagata	300
caaggtccga ataaaaggag gagaaaaatg ggtattaaat gtctaagaat tgggaggacc	360
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<210> 20

<211> 331

<212> DNA
<213> Homo sapien

<400> 20

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atctgcagaa cgatgcgggc attgtccaca gtatgtcgga agatctgagc cctcagggtcc	120
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<210> 21
<211> 346
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(346)
<223> n = A,T,C or G

<400> 21

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ctacatcctc actgactttc gcttggaaa cgtgttggga aaattgaggt gtttcattca	240
catctgtcac aataagnncgt gaacttggca aaagaacttg cattgtactt cacaccaaac	300
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<210> 22
<211> 360
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(360)
<223> n = A,T,C or G

<400> 22

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gagcagccac ctacttcaaa cccagcaccc gcagattgtc caggctgcgt cttagcacc	180
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caacttcaga tacagaagtt tacggtgagt tttatccgt gccacccccc tatagcgttg	300
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<210> 23
<211> 251
<212> DNA
<213> Homo sapien

<400> 23

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gaagtttggc tggatcaagg gtgtattagt acgttgtatg ttaaacattt ggggtgtatg	180
gcttttcatt agattgtcat ggattgtggg tcaagctgga ataggtctat cagtccttgt	240
aataatgatg g	251
<210> 24	
<211> 421	
<212> DNA	
<213> Homo sapien	
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<222> (1)...(421)	
<223> n = A,T,C or G	
<400> 24	
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ccggctcccg tgatgamcg ygggacctgy caswgctct gkttycctgc yagsacacca	180
cnytttyccg tggacacrar kggAACCKCT tgaaattcac agctyatgtt ctttctcara	240
agtttgagaa agaactttct aaagtgggg aatatgtcca attaatttagt gtgtatgaaa	300
agaaaactgtt aaacctaact gtccgaattt acatcatgga raaaggatac catttcttac	360
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c	421
<210> 25	
<211> 381	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(381)	
<223> n = A,T,C or G	
<400> 25	
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attttataact ttgcactaaa caaaaatagc ttatggaaaa ttatgttataa atagctaaac	240
acagaaaacc tacagctata aataacataa aatacagttt aactttatg ngatgctaa	300
acaaaagcaaa ctatgtgca atatgaatca acttcattaa ttggacaagt ccagnggagg	360
cacaaattag ataaggacta a	381
<210> 26	
<211> 401	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(401)	
<223> n = A,T,C or G	
<400> 26	
ggaaaaggga ctggcctctc tgaagagtga gatgaggggaa gtggaggag agctggaaaag	60

gaaggagctg gagttgaca cgaatatgga tgcagtacag atggtgatta cagaagccca	120
gaaggttcat accagaagcc aagaacgctg gggttacaat ccaagacaca ctcacacat	180
tagacgggct cctgcattct gatggaccaa cttttcang tggtaagatt gaaganggg	240
cctgggctta cctgggaagc aaaaactttt cccganccaa ggaacccagg attcaaccan	300
gcnacttgcn ggccaaggaa ggcanaactn ggaanaaaag gccccttaag caaaagggn	360
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<210> 27	
<211> 383	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1) ... (383)	
<223> n = A,T,C or G	
<400> 27	
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aaaaaaatat accacttcat agctaagtct tacagagaan aggatttgct aataaaactt	120
aagttttgaa aattaagatg cnggtanagc ttctgaacta atgcccacag ctccaaggaa	180
nacatgtcct atttagttat tcaaatacca gttgaggcgt ttgtgattaa gcaaacaata	240
tatttgttta aaccttgntt taaaattact gnntcttgac attacattata aaggagnctc	300
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<210> 28	
<211> 401	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1) ... (401)	
<223> n = A,T,C or G	
<400> 28	
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caatcaccat tggagaataa ctttattaa taagtgttat gagctctgctg acacttaccc	180
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<210> 29	
<211> 401	
<212> DNA	
<213> Homo sapien	
<400> 29	
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<210> 30	
<211> 401	
<212> DNA	
<213> Homo sapien	
<400> 30	
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<210> 31	
<211> 297	
<212> DNA	
<213> Homo sapien	
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<210> 32	
<211> 401	
<212> DNA	
<213> Homo sapien	
<400> 32	
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cctcctcaat ctggtttatg aaacaactga caaacaccc tctcctgatg gccagtatgt	300
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<210> 33	
<211> 401	
<212> DNA	
<213> Homo sapien	
<400> 33	
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<210> 34
<211> 401
<212> DNA
<213> Homo sapien

<400> 34
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<210> 35
<211> 401
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (401)
<223> n = A,T,C or G

<400> 35
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<210> 36
<211> 401
<212> DNA
<213> Homo sapien

<400> 36
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<210> 37
<211> 401
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1) ... (401)
<223> n = A,T,C or G

<400> 37
cnnctntgna atggantnnt tgnctaaaan ganttgatga tcatgaaanat ccctangang      60
antaagcatg gancntgatc nttncnng cactcctta cgacacggaa acangnatca      120
ncatgatggt accaganacc ttatcaccna cgcgcacnng nctgactnat tccaaagagt      180
tngngttacg gncatccggt cattgctcg tgcctattgt gcaggctga tnctactggt      240
gcttattatg ntggccctga ggatgctcca caatgaatat aagcatgctg catgatcagc      300
ggcaacanat gctctgccgt ttgcactaca tcttcacgg acacnatntc gaanacgggc      360
acnttgcana gttagacttg gaatgcatgg ngccggncan n                         401

<210> 38
<211> 401
<212> DNA
<213> Homo sapien

<400> 38
aattggctca ctctctcaag gcaaggactg tctcaaggca gtctcaaggc agagatgaca      60
cagcaaaaaa cagaggggggaa gaaaaaaagtc tattattggc ttgtgattta caaaagccaa      120
agtccttag ataaaaggcc aggagtctga ccaacataga taccaaatcc aggagaacac      180
agaccagcga taagagggac gcttccccat gacccagacc agcctaaagc ccctgtgggg      240
gcagccagtg gggagctgtc agaccttggc catgggtggc tttgagaatg ggtctgcct      300
tctctccctg accagttggg atagacacct gactggaatc cttgacactg gcaggtgttt      360
ctatgaacag agaggactgt gcctgtcttc ctgaatccca a                         401

<210> 39
<211> 401
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (401)
<223> n = A,T,C or G

<400> 39
tctggtangg agcaattcta ttatttggca ttgcatggct ggggtgaatt aaaacaggga      60
gtgagaacag gtgagtctag aagtccaaact ctgaaaagga ccactgtaca tttgaacaca      120
cggctgtgtt aaagatgctg ctaatgtcag tcactgggtg cactaaagga tctcttattt      180
tatgtaaaac gtgggaatg acaagatana actgatactc tggttaagtta ccctctgaag      240
ctacttcttg tgaataacta atgacagcat catcctgcac agcggaaagag gcaggcataa      300
gcaaggacaa attaaaaggg gttaagagcc ttatcatgat gaggagtctt gtttgacat      360
cttggaaaaa gctgtccata gtgtgaagtc gtcaatttct c                         401

<210> 40
<211> 401
<212> DNA
<213> Homo sapien

<400> 40
tctggtcacc caactcttgtt ggaagagggg aattgagatc gagtaactgaa tatctggcag      60
agaggctgga atccttcagc cccagagccc agggaccact ccagtagatg cagagagggg      120

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cctgcccagg ggtcagggca gtgggtatca ctggtgacat caagaatatac agggctgggg	180
aggcatctt gtttccttgt gcccttcata aagttgtcga cacttgggg acggaaagg	240
gtagaagttag ggctgctcct tttggagctg gagggaaatag acctggagac agagttgagg	300
cagtgggct gtccaggttc taagcatcac agcttctgca ctggctctg aggagattct	360
cagccagagg atcccagcct cctcctccct caaatgtcaa g	401

<210> 41
<211> 401
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(401)
<223> n = A,T,C or G

<400> 41

ctggactaaa aatgtccact atgggtgc ctctacagtt tttgaaatgc taggaggcag	60
aaggggcaga gataaaaaaa catgacctgg tagaaggaag agaggcaaag gaaacttagt	120
ggggaggatc aatttagagag gaggcacctg ggatccacct tttccttan gtccccctcct	180
ccatcagcaa aggagcactt ctctaattcat gccctcccga agactggctg ggagaagg	240
taaaaacaaa aaatccagga gtaagagcct taggtcagtt tgaaattgga gacaaactgt	300
ctggcaaagg gtgcganagg gagcttgc tcangagtcc agcccgcca gcctcggg	360
gtangttct gaagtgtgcc attgggcct caccttctct g	401

<210> 42
<211> 310
<212> DNA
<213> Homo sapien

<400> 42

ggttcgaccaa atccccaaaa atggcaaatt aagccctgtg aaaaaataag ttattggatc	60
atacagaaat agcccaaattc tggaaatttt gaattaaaat ttaatcctg taaaacaagt	120
tttgggtga atggatttct ttaataccaa taatattttt aattcccacc acagatggat	180
ttgctgaata tgctaattgtc gtgaatgaga aaacaattttt gggtaggtt tacccacaag	240
taatctgatg aaaaaataaaa ccacagactg atgtcaaattg gacaaaaaac tgaaaaatatg	300
ctgtgagaaa	310

<210> 43
<211> 401
<212> DNA
<213> Homo sapien

<400> 43

aggtcactta cacttgtgac cagtgtggg cagagaccta ccagccgatc cagtctccca	60
ctttcatgcc tctgatcatg tgcccaagcc agagtgccca aaccaaccgc tcaggagggc	120
ggctgtatct gcagacacgg ggctccagat tcatcaaattt ccaggagatg aagatgcaag	180
aacatagtga tcaggtgcct gtggaaata tccctcgtag tatcacggtg ctggtagaa	240
gagagaacac aaggattgcc cagcctggag accacgtcag cgtcactggt attttcttgc	300
caatctgctg cactgggttc cgacaggtgg tacagggttt actctcagaa acctacctgg	360
aagcccatcg gattgtgaag atgaacaaga gtgaggatga t	401

<210> 44
<211> 401
<212> DNA

<213> Homo sapien

<400> 44
atccctgtaa gtctattaaa tgtaaataat acatacttta caacttctct tagtcggccc 60
ttggcagatt aaatcttgc aaaattccat atgtgctatt gaaaaatgaa ataaaacctc 120
agatgtctga attcttattt caaatacagt tatataatta ttttaaatta caatatacaa 180
tttctgttaa atacaactgt taaggattc tgagaacaat tataagatta taataatata 240
tacaaactaa cttctgaaat gacatgggtt gttcccttc caccctccta ccctctcaa 300
gagttttgc atttgctgtt cctggttgca aaaggcaaaa gaaaatctaa aaatagtctg 360
tgtgtgtcca cgacatgctc gtcctttga gaatctcaa 401

<210> 45
<211> 401
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(401)
<223> n = A,T,C or G

<400> 45
gtgcctgctg cctggcagcc tggccctgcc gtcgcctcag gaggcgagg gcatgagtga 60
gctacagtgg gaacaggctc aggactatct caagagattt tatctctatg actcagaaac 120
aaaaaatgcc aacagtttag aagccaaact caaggagatg caaaaaattt tttggcctac 180
ctatactgga atggtaaact cccgcgtcat anaaataatg caanaagccc agatgtggag 240
tgccagatgt tgcagaatac tcactatttc caaatagccc aaaatggact tccaaagtgg 300
tcacctacag gatcgttatca tatactcgag acttaccgca tattacagtg gatcgattag 360
tgtcaaaggc tttaaacatg tggggcaaaag agatccccct g 401

<210> 46
<211> 401
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(401)
<223> n = A,T,C or G

<400> 46
gtcagaatttgc tctttctgaa aggaagcaact cggaatcctt ccgaactttc caagtcac 60
catgattcan agatactgcc ttctctctct ctgggatttt atgtgtttct gatagtgaat 120
tgttgatgta ttgctactt tgcttctttt ctctttcaag acttgatcat tttatatgtct 180
gnttggagaa aaaaagaact ttggtagca aggaggtttc aagaaatgat tttggatttt 240
ctgctgcgga atttctcgcc acctacctgt agtatggggc acttggttt gttcagagt 300
aagaaggtgg aagaatgagc tgtacttggt taagcagttg aaacctttt tgagcaggat 360
ctgtaaaagc ataattgaat ttgtttcacc cccgtggatt c 401

<210> 47
<211> 401
<212> DNA
<213> Homo sapien

<400> 47

ggctcgacgc aatgcacttc aaccatacat actgcttcca ctagctaata ccaaatgcag	60
gttctcagat ccagacaaat ggaggaaaag aacatttatg ctccgtttc agaaagccaa	120
gtcgttagtt tggcccttcc tttctctaaa gtttattccc aaaaacaggt agcattcctg	180
atgggcaga gaagaggata tttcagccc acatctgctg caggtatgtc atttctccc	240
atcttcactg tgacttagtaa agatctcacc acttctctt ggaatttcca actttgcttg	300
tgattgaatg tcacttcgtg aatttgtatt atgtcagatc acttggcatt gctctccat	360
atgcatacaag ttgccaggca ctaaacccaa tggcatgaa c	401
<210> 48	
<211> 430	
<212> DNA	
<213> Homo sapien	
<400> 48	
acataacttg taaactttt ctgcttgggg gctgtaacag acagaagagt aaagactaca	60
aggattttct gaagatgctt caatgaaaat catcatttcc tcttttagtca tcccaagtct	120
tggtttggaaa aacttggca tggacttata cagaccttga accaccactg acttattcatt	180
gggtggcaga ccttggaaacc aagctctctg tggacttctt gaaagtgeat caattctgtat	240
ttggcttaaga acagaagaca aatactggga tcgtgattct gtgttataact ctggccacag	300
catagcagct tctcgaacgg tttcttcctt ttctacattt aaattgtcac tactgagaat	360
atctatcagt aggtcatgtg acagacctgc cccggggccg gcccgtcga tgcttgccga	420
atatcatggt	430
<210> 49	
<211> 57	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(57)	
<223> n = A,T,C or G	
<400> 49	
ggtattaaca atatcangca ctcattttc ccctctttagt aaanggatna attttta	57
<210> 50	
<211> 327	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(327)	
<223> n = A,T,C or G	
<400> 50	
gatggnggtn tccacaagan tnaangtnn tattaantan nncttgtaga nccacttnna	60
ttaattgnnn tatgnntgnc cttctgggtgg ntgtngaagc ttcatatnnt ntttggacat	120
cattacacgt cttagcttt tnaagnacaa cttaatgtc atatgaattt tgccatttn	180
gctaacactg gtatgtccn ngcatccacc atnccacntg gaatttattt ttnccnttcat	240
attaatntt tgtttaccaa atctnacttg acccgaacga aactttctgn gtattttang	300
cccccnccat tcttactttt caagct	327
<210> 51	

<211> 236
 <212> DNA
 <213> Homo sapien

<400> 51

cgtctcgaaag aagcgctgca ggccgatgat ggactgcacg tctgccttgt cctcagttaa	60
cttggtaat tgcttgaaca tgcggcccac atccctggca aactcctgtg gggagctgt	120
gggaggtgac aacttctccct ggaggcggc acggatcagg gtcagatcca ggggccacc	180
gggctggtcc agggagaagg tggagtcgta gccagacctg cccggcggc cgctcg	236

<210> 52
 <211> 291
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(291)
 <223> n = A,T,C or G

<400> 52

ctcacatcct gggccggct gtagagctgc accatggtgc tgagcgcccc ctccagctcc	60
ttgttagatgt aaaggacggc gaaggagctg tagtctgtgt ccacgatgcg cacgtccagg	120
tagcccaagg ccgggactct gaagtgtcc ctccggagccc accttcangt actcgggcat	180
ccacctgggtt acagccnttc gncctcggnna actccatntg gactttacag gcccctcc	240
tctgtgggcc ttagtggncct tgcaggacat nggaacacgg gagtcnctt t	291

<210> 53
 <211> 95
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(95)
 <223> n = A,T,C or G

<400> 53

gtctgtgcag ttcttgacac ttgttgtga acatggntaa atacaatggg tatcgctgan	60
cactaagttg tanaanttaa caaatgtgct gnttg	95

<210> 54
 <211> 66
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(66)
 <223> n = A,T,C or G

<400> 54

cctnaatnat nttaatggta tcaatnnccc tgaangangg ganccggngga agccggnttt	60
gtccgg	66

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<210> 55
<211> 265
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(265)
<223> n = A,T,C or G

<400> 55
atctttcttc tcagtgcctt ggccntgttg agtctatctg gtaacactgg agctgactcc      60
ctgggaagag aggccaaatg ttacaatgaa ctaaatggat gcaccaagat atatgaccct      120
gtctgtggaa ctgatggaaa tacttatccc aatgaatgcc gtgttatgtt tttgaaaatc      180
ggaaacgcca gacttctatc ctcattcaaa aatctgggcc ttnctgaaaa ccagggttt      240
naaaatccca ttcnggtcnc cggcg      265

<210> 56
<211> 420
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(420)
<223> n = A,T,C or G

<400> 56
gagcggccgc ccgggcaggt cctcgccgtg acctgatggg atttcaaaac cttgggttctc      60
agcaaggccc agattttga atgangatag aagtctggcg tttccgattt tcaaaacata      120
acacgcattc attgggataa gtatccat cagccccaca gacngggtca tatatcttgg      180
gtgcattccat taagttcnnt tgtaaacatt tggccctetc ttccangg gaattcagct      240
cccagttgtt taccaanatt naactccacc gggccaaag gcnctgaaa aaaaaaanaa      300
ttccttggtt accttccttg ggcttnaagt tctggcgtcc aaaagttcaa tttgaaaact      360
gcaccgcact taccacgtct cttcnagaan cctggggaca cctcgccgc gaccacgcta      420

<210> 57
<211> 170
<212> DNA
<213> Homo sapien

<400> 57
gaagcggagt tgcagcgcct ggtggccgccc gagcagcaga aggccgagtt tactgcacag      60
gtgcattcaact tcatggagtt atgttggat aaatgtgtgg agaaggccagg gaatcgcccta      120
gactctcgca ctgaaaatttgc tctctccaga cctcgccgc gaccacgcta      170

<210> 58
<211> 193
<212> DNA
<213> Homo sapien

<400> 58
attttcagtg cgagagtcta ggcgattccc tggcttctcc acacatttat cccaaacataa      60
ctccatgaag tcatggcacct gtgcagtaaa ctgcgccttc tgctgctcggtt cggccaccag      120
gcgcgtcaac tccgcttcat cggcttcggcc cagctccggcc attgttcggcc acctgccccgg      180

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gcggccgctc gaa	193
<210> 59	
<211> 229	
<212> DNA	
<213> Homo sapien	
<400> 59	
cgcaactctc gagcatttat atacaatagc aaatcatcca gtgtgttgc cagtctataa	60
tactccaaca gtctccatc tgtattcaat ggcgccaccc aatacagtcc tttgtttgga	120
tgctggggag agtaatccct accccaaggca ccatatatagat aagaaaaccc tctccagttg	180
agctgaacca cagacggttt gctgataacct gcccgggcgg ccgctcgaa	229
<210> 60	
<211> 340	
<212> DNA	
<213> Homo sapien	
<400> 60	
tcgagcggcc gcccgggcag gtcctctaaa gatcaaaaca cccctgtcgt ccaccctcct	60
cccactccag ggaagctgtg gtcatggtgg tgtggtaaac atcagcaaac cgtctgtgg	120
ttagtcaac tggagagggt ttctttatct atatggtgc tgggttaggg attactctcc	180
ccagcatcca aacaaaggac tgtattgggt ggcgccattt aatacagatg ggaaactgtt	240
ggagtattat aaactggtac aacacactgg atgatttgc attgtatata aatgctcgag	300
aattgcggat cacctatgga ctcggccgc gaccacgctg	340
<210> 61	
<211> 179	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(179)	
<223> n = A,T,C or G	
<400> 61	
tttttgtac ggacgnttgg agtacatgtc ccaggatcac atccagcagc tagagtggct	60
gggacaagct ggcggnggc aagcactgtt gaaacnatag gggctgggn gnactcggt	120
ttaaagtggtt ggtccgantn ttnataacct tgcngaaacc nancatctcg gttgncang	179
<210> 62	
<211> 78	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(78)	
<223> n = A,T,C or G	
<400> 62	
agggcgttcg taacggaaat gccgaagcgt gggaaaaagg gagcgggtgc nggaagacgg	60
ggatgagctt angacaga	78

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<210> 63
<211> 410
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(410)
<223> n = A,T,C or G

<400> 63
cccagttact tggggaggct gaggcaggga gaatccttg aacccggngg gtgggaggtt      60
gcagttagcc cgagatagca ccattgcact tccancatgg ggtggacaga gtgagactct      120
atctcaaaaa aaaagaaaag aaaagggaaag agattagatt aagattaagt acctacttcc      180
tntcccattt caagtcctga aaatagagga tcagaaatgt tgaggaattc tttaggatag      240
aaagggagat gggattttac ttatgggaa agacccgcaaa taaagactgn aacttaacca      300
cattccccaa gtgnaaggtg ttacccaaga attaggaacc cttttggctn ttaccttacc      360
ttccngaaaa aaaccttattn cttaaaatgg aaacccttaa agccccggca      410

<210> 64
<211> 199
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(199)
<223> n = A,T,C or G

<400> 64
cttgttctca aaaaggtcaa agggagcccg acgaggaata aatagcaatg cccctgaattc      60
caactgacct tctacagaaa agtgcttgac tgccaaagtgg tcttcccagt cattagttag      120
gctctttag aattctccat actcctcttg ggrngangnca tnagggtttngggccaaat      180
aggntgggcc tngttaagt      199

<210> 65
<211> 125
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(125)
<223> n = A,T,C or G

<400> 65
agcggtacag ttctgtcctg gcatcatcat tcattgttagt atggtaata ggtgccatga      60
aactcagtag cttgctaagg acatgaaacc gaagtttcct gccttgctg gcctngtng      120
gggta      125

<210> 66
<211> 204
<212> DNA
<213> Homo sapien

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<400> 66
 attcagaatt ctggcatcggtat tttctata aagtccatca gtttagagcag gagcaggccc 60
 ggagggacgc cctgaagcag cggcgaaac agagcatctc tgaagagccc ggctgggagg 120
 aggaggaaga ggagctcatg ggcatttcac ccatatctcc aaaagaggca aaggttcctg 180
 tggacctcggtcgaccac gcta 204

<210> 67
 <211> 383
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(383)
 <223> n = A,T,C or G

<400> 67
 tcagggcctc caggcagcca gtttgcagg anattcagca cctagngtct tcctgcctna 60
 cgctccaaag aacctgctcc tgcaaaaaa acatcagaac tcgtccttga tgtcaaaatg 120
 gggctggctct tnaggcttga agtccaggtt agggctgcca tcctcattga gaattctccg 180
 ggcagtgtaan ccgacatgg ggtatttggc ttgtacact ttggtaaaaa cctnatccag 240
 ggcctccagt tccttggccg tganaccgt antgtcatgg gtgaggtctg caggatccaa 300
 ggacatcttgcgtacccctc tagtggatgc cttccccgtc aaggcattgt aaggggctcc 360
 tcgtccataaa aactcctttt cggt 383

<210> 68
 <211> 99
 <212> DNA
 <213> Homo sapien

<400> 68
 tcacatctcc tttttttttt aacttttca aattttgtt ttaaatagaa ggctaaaggg 60
 ttagatttaa gtttctgcta cattgaccct atttaccta 99

<210> 69
 <211> 37
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(37)
 <223> n = A,T,C or G

<400> 69
 gagaaggacn tacggncctg ntantanang aatctcc 37

<210> 70
 <211> 222
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(222)

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<223> n = A,T,C or G

<400> 70
gtgggtcatt ttgctgtca ccagcaacgt tgccacgacg aacatccttg acagacacat      60
tcttgacatt gaagcccaca ttgtccccag gaagagcttc actcaaagct tcataggcgca     120
tttcgacaga ttttacttcc gttgtaacgt tgactggagc aaagggtgacc accataccgg     180
gtttgagaac acccantcac ctgccccggg cggccgctcg aa                           222

<210> 71
<211> 428
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(428)
<223> n = A,T,C or G

<400> 71
caggagtatt tttagaaaaa gccagaagag cattagtaga tgtatggaaa tatacggtag      60
ggcacacgct gacagtactt ttcccaagcc acgcccgtatt tcttcttaca gtggtactcg    120
tcacgagctt ctcgggtggac aagcaacatg gtgaaataaa ttatgttagaa ataaggcaga    180
atgtggtaa aaccacatgg gagggaccac gccaaggcca tcatgagatc acccaagtaa    240
ttgggggtggc gaacaaaagcc ccaccatcca gaaactagaaa naattttcc cggtgaaata   300
tgaatggntt taaaatgtgc aagcttggaa tcactgggaa tttcccgaa tgccttttc     360
tganaattgc accttnggaa gantccttac cccaaagnttc agaccattat ttnaaaagcn   420
ttggaact                                428

<210> 72
<211> 264
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(264)
<223> n = A,T,C or G

<400> 72
gaataaaagag cttaactggaa tccagcaggg ttttctgcc aaggatttgc aagctgaagc      60
tctctgcaaa ctgtatagga gagtaaaaag ccacaataga gcagtttatg aagatcttgg    120
aggagattga cacacttgc cctgccagaa aatttcaag acagtagatt gaaaaggaaa    180
ggcttggta aaaaaaggtt caggcattcc tagccgantg tgacacagtg gagcanaaca    240
tctgcangag actgancggc tgca                                264

<210> 73
<211> 442
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(442)
<223> n = A,T,C or G

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<400> 73
 ggcgaatccg gcgggttatca gagccatcg aaccgccacc atgacggtgg gcaagagcag 60
 caagatgctg cagcatattg attacaggat gaggtgcatt ctgcaggacg gccggatctt 120
 cattggcacc ttcaaggctt ttgacaagca catgaatttg atcctctgtg actgtatga 180
 gttcagaaaag atcaagccaa agaactcaa acaagcagaa agggaaagaga agcgagtct 240
 cggctctggng ctgctgcca gggagaatct ggtctaatg acnntagaag gaccttcttc 300
 caaagatact ggnattgctc gagttccact tgctggaaact tcccggggcc caaggatcgc 360
 aaggcttctg gcaaaagaaa tccanacttn ggccgggacc acctaancctt attcacacac 420
 tggcgccgt actagtggat cc 442

<210> 74
 <211> 337
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(337)
 <223> n = A,T,C or G

<400> 74
 ggttagcagcg tctccagagc ctgatctggg gtccccagata cccaggcagc agcagccctg 60
 gaggtaaagg gcaagctccc .aatgtgagg ggagacccca ttccctggta gccaggctt 120
 cagaggagat agcaggtcga gggagccaaac gaagaagaga ctgccancag gggaggact 180
 gtccccccaa ggacagaact gattcagggg ggtcaatgt cctctagaga agagccacac 240
 agaactgggg ggtccaggaa ccatgaanct tggctgttgt ctaaggagcc aggaatctgg 300
 acagtttctt gggtcatacc aggattctgg aattgtt 337

<210> 75
 <211> 588
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(588)
 <223> n = A,T,C or G

<400> 75
 catgatgagt tctgagctac ggaggaaccc tcatttcctc aaaagtaatt tattttaca 60
 gcttctgggtt tcacatgaaa ttgttgcgc tactgagact gttactacaa actttttaag 120
 acatgaaaag gcgtaatgaa aaccatcccg tccccattcc tcctcctctc tgagggactg 180
 gagggaaagcc gtgttctga ggaacaactc taatttagtac acttgtgttt gtagatttac 240
 actttgtatt atgttataac atggcgtgtt tattttgtt tttttctctg gttgggagta 300
 tgatatgaaat gatcaagatc ctcaactcac acatgttagac aaacatttagc tctttactct 360
 ttctcaaccc ctttatgtt ttaataatt ctcacttaac taattttgtt agcctgagat 420
 caataagaaa tgttcaggag agangaaaga aaaaaaaatat atgtcccca ttttatattt 480
 gagagagacc cttantctt cctgcaaaaaa gtccacctt catagtagta ngggccacat 540
 attacattca gttgctatag gncagcactg aactgcattt cctgggca 588

<210> 76
 <211> 196
 <212> DNA
 <213> Homo sapien

<400> 76

gcggtatcac	agcctggccc	ccatgtacta	tcggggggcc	caggctgcc	tcgtggctca	60
tgacatcacc	aacacagata	cattgcacg	ggccaagaac	tgggtgaagg	agctacagag	120
gcaggccagc	cccaacatcg	tcattgcact	cgcggtaac	aaggcagacc	tggacctgcc	180
cgggcggccg	ctcgaa					196

<210> 77

<211> 458

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(458)

<223> n = A,T,C or G

<400> 77

agtagagatg	gggtttca	gtgttaacca	ggatggtctt	gatctcctgg	cctcggtatc	60
tgccccgc	ggcctccaa	agtgtgg	ttacaggcg	gaaccaccgc	acccggccag	120
aatgttagt	ttttccctat	tctctctc	ttttcctatt	atatacttgg	tcaaccagac	180
agccatccta	ccccanaatg	gtaatgc	ttcattc	atatgaggga	ataaaagaga	240
aaaaagctt	tggaaaacat	ccacttatct	aatcatccc	aatatgtat	caaaagtata	300
caactcatgt	gaagaataca	ctggtaaaat	gttanta	tag gccaa	gttcat	360
tatataaaaa	gctgttaat	gccctttgg	ctggaaaccgc	catttccnn	taattcnccc	420
aaaatgacca	aacacaaagg	gnaagangan	aagcccc			458

<210> 78

<211> 464

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(464)

<223> n = A,T,C or G

<400> 78

tccgcaaatt	tcctgcccgc	aaggcccag	catttgagg	tgtatgtatgg	ttctgtgtgt	60
ttgagagcaa	cgcattgc	tactatgt	gcaatgagg	gtgcgggg	agtactccag	120
aggcagcagc	ccagggtgt	cagtgggt	gctttgctg	ttccgatata	gtgccccccag	180
ccagtagct	gggtttcccc	accttgg	tcatgcacca	caacaacag	gccactgaga	240
atgcaaagg	ggaagtgg	cgaattctgg	ggctgctgg	tgcttacttg	aagacgagg	300
cffffctgt	gggcgaacga	gtgacattgg	ctgacatcac	agttgtctgc	accctgttgt	360
ggctctataa	gcaggntcta	gaaccttctt	ttcgcangac	cttcggccgg	accacgctta	420
acccaaattc	cacacacttg	cngccgtac	taanggaatc	ccac		464

<210> 79

<211> 380

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(380)

<223> n = A,T,C or G

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<400> 79
ctgtatgacc agttttcca ttccttcac ttctaccttg atcagctcg agtccagttc      60
agtgtaaaga atggtatcct tctccatgt gtcattcgg acagtaggt ttaacagtt      120
ctttcatac acactaatta attggacata ttccctca cttnaaagtt ctttctcaa      180
cttctganaa aagaacatga actgtgaatt ccaagcgttc ccactctgtc cacgggaaa      240
ggtgtgtct ggaggaaa cagaacactg gcaggtccac ggtcatccac ggagccggtg      300
aaattggaa aacaactgg acacagaacc tccgctgcct aagctgcgn tggagcttg      360
gaacccgacc tggactgga      380

<210> 80
<211> 360
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(360)
<223> n = A,T,C or G

<400> 80
tcgagcggcc gcccggcag gtcctcagag agctgttgt tncgcttctt caaaaactcc      60
tattctccac ttctgctaaa ggactggatg acatcaattg tgatagcaat atttgtgg      120
gttctgtcan ncancatcg actcctgaac aaagtagatg ttggattgga tcagtcttt      180
tccacccaga tgactcctan atggtgatn atttcaaatac catcantcag tacctgcatg      240
cnggtccgc ctgtgtntt tgcctgcag ganggcnc actacactc ttccnagggg      300
canaacatgg tgtcngcgg ccatggcgtg gcaacantga ttcnctgctg cacccanatn      360

<210> 81
<211> 440
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(440)
<223> n = A,T,C or G

<400> 81
acgtggtccg gcgagtctga cctgcagata tgaactcctt gggaaaccta cattctgcct      60
cagacatact gggggcaaat ggcttaaaa gtctggctca gggagccaag attacagaaa      120
nccgttgagt cnccatacat ggacactgac aaaggaactg aagatatcca aacaagccct      180
cctggtcccngcctgcata aagatcgggncggaaacgggt accngacgtc tgggtcagg      240
ggttgtggaa aattggaaaa aaccagtctt ccccacattg acagggaagc ctcaacggaa      300
attgaacaga tngtcttaccaggctcc cctcctgat cngtctcggt ctcnngggan      360
tcagtgtatca gtcctttagt gttggaaagaa caaagaagat caacaanaag cngatcctct      420
cacctgntac cagcatatgg      440

<210> 82
<211> 264
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature

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<222> (1)...(264)
<223> n = A,T,C or G

<400> 82
agcgtggtcg cggccgangt cctgacattc ctgccttctt atattaatta tacnaataaa      60
acaaaatagt gttgaagtgt tggagcggcg aaaattttg ggggggtggta tggacagaga     120
atggcgatn ttctcanggc tgcttcaagt gggattgggg cnngcgtggga tcatncagtg     180
ggnanagatn cnctgaccgg antctnttgg tanggatnat cttgtggggta tgtgcaagag    240
ncattcgctc cctgaatgan tggt                                264

<210> 83
<211> 410
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(410)
<223> n = A,T,C or G

<400> 83
ancgtggtcg cggccgangt ccacagttgt gggagagcca gccattgtgg gggcagctcc      60
acaggtaaga ctcgtgtcct gagcagcga catcatccag gacaatgggt cctgagccct     120
gaccAAaccg ggcatTTccct ggggctgaca tggcccagcc acagcccant tgcctgcaga     180
cgAAattggc atcatTTgtg tcccagtant catcacacac ggtgccccag gaacctccgg     240
tatangaact ccaactcgcc tcnanacctg tcgcctccat tccncagcct cagggggcaa    300
actgggattc agatccttct gtgggtacag gtgggtatat cctgacaggc caactttctg    360
gcctgagtgt tgactgangc tggcagacc tgcccgccg gcccgtcga                               410

<210> 84
<211> 320
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(320)
<223> n = A,T,C or G

<400> 84
tcgaacggcc gcccggcag gtctgccccca ggtgtatcca tttgccggccg atctctatca      60
naaggagctg gctaccctgc nnncgacgaan tcctgaanat aatctcaccc ncccagatct     120
ctctgtcgca atggagatgt cgtcatcggt ggnccctgatc acagggcatt ggactcagag     180
anangtnanc acagtgtnga agcgattgan nnagttcagt tgctggctt acccgatntt     240
ggaaggaagg aaaacgtgtt angacgtatc tcgatgnant tgaccaaanc tgaangctnc    300
agggggcattc gcaaaganan                                         320

<210> 85
<211> 218
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(218)

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<223> n = A,T,C or G

<400> 85
tcgagcggcc gcccgggcag gtctgctgcc cggtgctggtg ccattgcccc atgtgaagtc 60
actgtgccag cccagaacac tggtctcggtt cccgagaaga ctcccttctc caggctntan 120
gtatcaccac taaaatctcc aggggcacca tnganatcct gggtgtccgc aatgttgcca 180
atgtctgtcc gcnnattggc tacccaactg ttgcatca 218

<210> 86
<211> 283
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (283)
<223> n = A,T,C or G

<400> 86
tcgacttctt gtgaagggttt tgganaaaata tgtatcagtt cggttttattt gggatttcaa 60
taatatccctt ggtgataatgt ctgactccat ggcttctgac cccaaaaatt gaccctgctg 120
ccactggtt tagccctgag attgattttt gtagccacga ttgtttcctc gtcctctgaa 180
gtntctgttg tanttccctc tgnngggcat tcccctctgt tgtanttccc tctgtttgan 240
taactaccac ggccagggaaa aacaggggca cgaaggatgt gat 283

<210> 87
<211> 179
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (179)
<223> n = A,T,C or G

<400> 87
agcgtggtcc cggccgatgt ctttctgtgt aagtgcataa cactccacat acttgacatc 60
cttcangtca cggggccagct nttagtcaatc ctctggatgt ataggctact gtntgttctn 120
ggcaagtgtc tcaanaatac aggggtcnc tctgagatga nttagtcc cgaaccctc 179

<210> 88
<211> 512
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (512)
<223> n = A,T,C or G

<400> 88
tcgagcggcc gcccgggcag gtcctancan agaatcacca aatttatggaa gagttAACAG 60
gggtttaaca ggaangaagt gccttagta agttctcaag ccagangctg gaggcagcag 120
ctaaatcaga ggacaggatc ctcagtggaaa gtgagccatt cgggggtggca tgtcactcca 180
ggaataagca caacttanaa acaaattgatt tcgtangata gcacagtgcatttgcac 240

ttgtgaacct gaggccactg tgtcaaactg tgcactgggt gtgaataggg aganccaaaa	300
attatgtcct actggtaat gagcttcaa tgggctcgat cctctcacnc taaaagctct	360
gttagagcagc tcagaaccac aaccactccc aacattgacc cttctgggg tactgtctgt	420
ggcacccaca ggaaggagct ggagatcccc attaggactg tccacccaca cttgaaggcca	480
caaaactgca cctcgccgc gaccaccgct ta	512
<210> 89	
<211> 358	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1) ... (358)	
<223> n = A,T,C or G	
<400> 89	
tcgagcgggc cgccgggca ggtctgccag tccccatccc agacattctt tgcatactaa	60
ctgangtctg aactgagtgg ggtgggctgg ttttccatc ctcacaactc cagttagccg	120
ggtgtggccg tggctgcgt ctctctggcg gtttagtcatg ttggcatcat ccaccccttt	180
caaaacaaaaa gcactggact gaagaanaat cccnccctgt ntccacccag tccatggttt	240
ttaataaaaag gtttatnnaa gttgancaag ncatacaccac acacaancct aagaacnttt	300
ttcatcnntc cccaaaacaa acccnccaccc tggaactcc gggcgcaac cacgccta	358
<210> 90	
<211> 250	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1) ... (250)	
<223> n = A,T,C or G	
<400> 90	
cgagcggccg cccgggcagg tctggatggg gagacggact ggaactgcgg cttcccggtgg	60
cctgcacgca caaggctccc cacggccccc gaccttcttc agattcgatc gtatgtgtac	120
gcacnaagag ccaaataattg acattcacaa ctctgtggga atnttacccc anaagactgc	180
gaccccccga tcagggcgana gcctgagcat agaagaacac cgctgtgggc ttggcactgt	240
gggncccatc	250
<210> 91	
<211> 133	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1) ... (133)	
<223> n = A,T,C or G	
<400> 91	
tcgagcggcc gnccgggcag gtcccggtg gttgttgcc gaaatggca agttcntnaa	60
ncctggaaag gtggtgcntg tnctggctgg acgctactcc ggacgcnaag ctgtcntcgt	120
gangancatt gat	133

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<210> 92
<211> 232
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(232)
<223> n = A,T,C or G

<400> 92
agcgtggtcg cggccgangt ctgtcacttt gcggggtag cggtcaattc cagccaccag      60
agcatggctg taggggcgtat ctgaggtgcc atcatcaatg ttcttcacga tgacaagctt     120
tgcgtccgga gtagcgtcca gccaggacaa gcaccacctt cccacgtntt cangaactng     180
cccatttcgg cataaccacc cgggacctgc cgggcggnc gtcgaaaag cc                232

<210> 93
<211> 480
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(480)
<223> n = A,T,C or G

<400> 93
agcgtggtc gcccgcgang tctgtangct caccggccag agaagaccac tgtgagcatt      60
ttgccgtata tcctgcctgt ccatttttc actttttaaa ctaaaatagg aacatccgac     120
acacaccgtt tgcatcgctc tctcccttga tattttaaagc atttttccat gtcgtgagtt    180
tctcagaaac atgtttttaa caattgtact atttagtcat ngtccattta ctataattta   240
tctgaccatt tcctactgt taaaatactt aagacggttt ctgatttttc cactatttaa   300
ataatgctgt gatgaatatc tttaaaatct tctgattttct tacttttttc ccccttagat 360
gcctgaaagt ggtattttga ggtgaaagag tttgttcatt ttgaanatat ttctgtctct 420
ctctcgacct gatgtgtana cgctcaactc cagtttagcag aaccacctta gtttgtgtct 480

<210> 94
<211> 472
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(472)
<223> n = A,T,C or G

<400> 94
tcgagcggnc gccccggcag ggtctgatgt cantcacaac ttgaaggat gccaatgtat      60
taccaatccn atgtgaaatc tctcccttta tctccatgc tgganaaggg attacaaagt     120
tatgtggcng ataannaatt ccatgcacct ctantcatcg atgagaatgg agttcatgan   180
ctggtaacn atggtatctg aaccgatac cangttttgt ttgccacgt angantagct    240
tttatttttg atagaccaac tgtgaaccta ccacacgtct tggacnaactg anntctaact 300
atccncaggg ttttattttg cttgttgaac tcttncagct nttgcaaact tcccaagatc 360
canatgactg anttcagat agcattttta tgattccan ctcattgaag gtcttatnta 420

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tntcnntttt tccaaagccaa ggagaccatt ggacctcgcc cgccgaccacc tn	472
<210> 95	
<211> 309	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(309)	
<223> n = A,T,C or G	
<400> 95	
tcgagcggcc gcccgggcag agtgtcgagc cagcgctgcc gcgtatgggtgt tggtggagag	60
cgaggcgttc ctgacggAAC tgaccagact ttccanaag tgccggacgt cgggcancgt	120
ctatatcacc ttgaagaant atgacggtcg aaccaaaccC attccaaaga aangtactgt	180
gganggcttt gancccgcaG acaacnagtG tctgttaaga actaccgatn ggaaanaana	240
anatcagcac tgggggtgag ctccnaggGA agttaataan ttccggatgg gcttattcna	300
accccttta	309
<210> 96	
<211> 371	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(371)	
<223> n = A,T,C or G	
<400> 96	
tcgagcggcc gcccgggcag gtccaccact cacctactcc ccgtctctat agatTTgcct	60
gttctggca gtTCTcagca atggaatcct actgtgtatC tttttgtgac tggttcttta	120
actcagcatc acatTTCAA ggttcatcca tgctgcagCC tggctccgta ctgggtgacAG	180
tacttcattt ctctctccct tttgttcaga ccaaggTctc cctctgtccc caaggctaaa	240
gtgcagttgg tggatcatg gctcaTGca gcctcaaact cctggactca aacagtccTC	300
ccatctcagc ctcccaaAGt gctgatntta taagttgcaa gccctgcacc cagcctgtat	360
ctccagtttG t	371
<210> 97	
<211> 430	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(430)	
<223> n = A,T,C or G	
<400> 97	
tcgancggcc gcccgggcag gtttnttttN tttntttttt nnnngntagt atttaaagan	60
atttattaaa tcatcttATC accaaaatgg aaacatnttc caactagaaa catgcnaCCA	120
tcatcttccc cagtccagtc ncaangtcca atatTTnCT tgccTCTGca gataaaaAGt	180
tcnnattttt atacccactc ttactccccC caaaaatttt aattcngtcc tnccctaaaa	240
ttncnccggg taacaantta caaaaatggc naaccaatta ttttaaanaaa aagttgcncn	300

ttnaaaangg aaactttntg gcaanttanc ctctttccc ttcccacccc ccanttaag	360
ggaaaaacaa tggactttg ctctgcttn aacccaaaat tgtctccaa aaactattaa	420
aatgttnaa	430
<210> 98	
<211> 307	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(307)	
<223> n = A,T,C or G	
<400> 98	
tcnaacggcc gcccnngcnn gtctngcngc acctgtgcct canccgtcga tacctggtcg	60
attgggacan ggaanacaat ntggtttca gggaggccac anattggag aaacggatga	120
attctcctt atccgaant cagctccttg gtctccgtag anggtgatct taaaatttgc	180
ctgtttgaa aactttcttg aanaaacctt acctgctggt tgtatttggt ctcccactcg	240
gacaagtact cgatatccnn ggtactctta atgtgccac gttaactccc cgggntggca	300
actggaa	307
<210> 99	
<211> 207	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(207)	
<223> n = A,T,C or G	
<400> 99	
gtccnnggacc gatgttgcna aganntttct tggccanta ggttcnaaaa aatgataanc	60
naggtntanc acgtgaagat ntntatanag tcttantnaa aacncntaga tctgnatgac	120
gataantcga anacnggggg aggggntgag gngaggtggn gtganggaag anntgttcat	180
aaaagannna gntgataaga anngagc	207
<210> 100	
<211> 200	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(200)	
<223> n = A,T,C or G	
<400> 100	
acntnnacta gaantaacag ncnttctang aacactacca tctgtnttca catgaaatgc	60
cacacacata naaactccaa catcaatttc attgcacaga ctgactgtaa ttaattttgt	120
cacaggaatc tatggactga atctaattgcn nccccaaatg ttgttngttt gcaatntcaa	180
acatnnttat tccancagat	200
<210> 101	

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<211> 51
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(51)
<223> n = A,T,C or G

<400> 101
tcgagcggcc gccccggcag gtctgaccag tgganaaaatg cccagttatt g      51

<210> 102
<211> 385
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(385)
<223> n = A,T,C or G

<400> 102
aacgtggtcg cggccgaagt ccatggtgct gggattaatc cactgtgacn gtgactctga      60
gtttagtgtt tttcaatct tctccaagcc tgtggactca tcctccacat cttgggttag      120
taggatgaac atgctgaaga tgctnatttt gaaaaggaac tctatgaatc ttacaattga      180
atactgtcaa tgttccccca tnacagaacg tgncccccac aggttccatc atctgcactg      240
ggtttgggtg ttctgtcttg gttgactctt gaaaaggac atttctttt gttttcttga      300
attcangaa attttcttca tccactttgc ccacaaaaagt taggcagcat ttaacccca      360
anggattttg ggtctgggtc ctgcc      385

<210> 103
<211> 189
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(189)
<223> n = A,T,C or G
<400> 103
agcgtggtcg cggccgaagt ctgcagccctg ggactgaccg ggaagctctg attatcc      60
caccacaggt angttgtgtt ctgaatctca agttcacagg ttaaggctac agcatactca      120
tcctccacgg ggtggantt gttgctggtg atgaanggtt tgggggtggct ctgcataact      180
gttgatctc      189

<210> 104
<211> 181
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(181)
<223> n = A,T,C or G

```

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<400> 104
tcgagcggcc gcccgcccag gtccaggctc ccaccaangc accaccgtgg gaagctggta      60
attgatgccc accttgaagc cncntggggca ccatccncca actggatgct gcgcttggtt      120
ttgatggtgg caatggcaca ttgactctt tggaaaccac ttcaccacgg tacaacaggc      180
a                                         181

<210> 105
<211> 327
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(327)
<223> n = A,T,C or G

<400> 105
tcgagcggcc gcccgcccag gtcttctgtc gagtctgcgt gggcatcgtg ggcagtgggg      60
ctgcccctggc cgatgctcan aaccccagcc tctttgtaaa gattctcattc gtgganatct      120
ttggcagcgc cattggcctc tttggggta tcgtcgcaat tcttcanacc tccanaatga      180
anatgggtga ctanataata tgtgtggtn gggccgtgcc tcacttttat ttattgctgg      240
ttttcctggg acagaactcg ggcgcgaaca cgcttancgg aattccaaca cactggcggg      300
cgttactagt ggatccgagc tcggtagc                                         327

<210> 106
<211> 268
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(268)
<223> n = A,T,C or G

<400> 106
agcgtggctcg cggccgangt ctggcgtgtc ccacatcggt cccacctcgc tttacaaaac      60
agtccctgaac ttnatctaattt aaaaatttattt tacacnacat ttacattttaga aaaaganagc      120
tgggtgtang aaaccgggccc tgggtttccc tttaaagcgaa ngtggctcca cagttggggc      180
atcgctcgctt cctcnaagca aaaacgccaa tgaacccna agggggaaaa aggaatgaag      240
gaactgnccn gggangnccg ctccgaaa                                         268

<210> 107
<211> 353
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(353)
<223> n = A,T,C or G

<400> 107
tcgagcggcc gcccgcccag gtggccaggc catgttatgg gatctcaacg aaggcaaaca      60
cctttacacn ctagatggtg gggacatcat caacgcctg tgcttcagcc ctaaccgcta      120

```

ctggctgtgt gctgccgcag gccccagcat caagatctgg gatttanagg gaaagatcnt	180
tgtnnatgaa ctgaancnta aattatcagt tccannacca ngcaaaaacc acccnngtgc	240
ctccctggcc tggctcgctg atgggacctc gggcgcaac acgctnancc caattccanc	300
acaactggcg gncgttacta ntggatccga actcnggtac caancttggc gtt	353
<210> 108	
<211> 360	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(360)	
<223> n = A,T,C or G	
<400> 108	
agcgtggtcg cgccccagaat cctggcctca catgaccctg ctccagcaac ttgaacagga	60
naagcagcag ctacatcctt aaggccggaa aagtttagatg aagatttggaa tcctgcattt	120
ncctgcctcc cacctatctc tcccnaatta taaacagcct ctttggaaag cagcagaatt	180
aaaaaactct cccnctgccc tnttgaacta cacaccnacc gggaaaacct ttttcanaat	240
ggcacaaaaaa tncnaggaa tgcattcca tgaangaana aactgggtta cccaaaaatta	300
ttgggttggg gaaatccnngg gggggttttn aaaaaaggc aanccnccaa anaaaaaaac	360
<210> 109	
<211> 101	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(101)	
<223> n = A,T,C or G	
<400> 109	
atcgtggtcn cgccccagaat cctgtgtcct ggatggcccg tgtgcancga atccgttggc	60
gactcctaac taccaaaaaa angactctcg gaagaaaattt c	101
<210> 110	
<211> 300	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(300)	
<223> n = A,T,C or G	
<400> 110	
ccangggaaac ccagagtcac atgagatagg gtggcttcg ggacaggggg tcagangaat	60
ggtacatgga tctcagcccc tcatggacac ggaacaggtg tggtcagaac tcccangatt	120
ctgcatccan gatccagtct ctatagaagt tatggatcat tccttcattt cattcccccc	180
ttcatgaaaa aacttctgaa caagcccttt ttctcacttt gggccctgt ttggcncaag	240
gtnttnantt gggaaaaaaa aaacaaatcc ntccnttan ccctccgtgg ggaatgac	300
<210> 111	

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<211> 366
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(366)
<223> n = A,T,C or G

<400> 111
cgagcggccg cccgggcagg tccttgcgtt gccatctgtt ancattgatt tctggaatgg      60
aacancttc tcaaagtgg gtcttgctan tcatgaagtgc atgtcagtgt cttaagtac          120
tgctgctcac ttcccttaccc agggaaatata ctgcataagt ttctgaacac ctgtttcan      180
tattcactgt tcctctcctg cccaaaattg gaagggaccc cattaaaaaa tcaaatttga      240
atcctgaaan aaaaacngga aatntttctc ttggaattttg gaatagaatt attcanttga      300
ataacatgtt tttccccctt gccttgctct tcncaanaac atctggaccc cggccgcgac      360
acctta                                         366

<210> 112
<211> 405
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(405)
<223> n = A,T,C or G

<400> 112
ctgactncta aacttctaatt tcnatcaana taactactct cttccgtct tncagagtgt      60
tcacaataaa tctgtgaatc tggcatacac agttgctgga aaattgttct tcctccacna      120
aaaggtcaat tggcnccnc atgaaanaag ataaatttgtt catccatcac tnctgaacca      180
tccaaaacgc cggcggaaatt attnccccgt tattatgggg aacgaaattt tnaataaaatt      240
tgggaangaa tggggctttt attgtttgt tttccccctt tcttggcatt gattggccg      300
caatggggccc cctcgctcan aanntgcccc ggggcccggcc gctccaaaac cgaaattccc      360
anccacactt ggcggggccgt tactanttgg atccgaactc ggtta                         405

<210> 113
<211> 401
<212> DNA
<213> Homo sapien

<400> 113
ggatagaaga gtatatgggt ttggcaccac ggggtggata ggcaaaacat ttggttgata      60
aggcgcagat tctgaactaa cttgttaaggc ttgtctgggtt ttaggacagg taaaatgggg      120
gaatggtaag gagagtttat aggttttagg agcccatgtt gtagcaggca agtgataaca      180
ggcttaatc cttcaaaggc atgctgtggg atgagatatt ggcatttgag cgggtaagg      240
gtgatttaggt ttatgttggg tggtaagggg tgcattatcc ggtccgccaa ggaagggaag      300
tagaggtatc ttatacttgtt ggggttaagg tgggggggat ataagaggga ggacgccaagg      360
ggaggcttg gatttaggaat aaggggcggc aatgagatgc a                                         401

<210> 114
<211> 401
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(401)
<223> n = A,T,C or G

<400> 114
angtccacag gangcangag gccaggctcc gtcccancctt gtccatgatg ttgaagagga      60
ggaaggcagca catgggtttt aagaactgac tccacttccc aggactggtg gagctggta      120
ccatggctgt ggtggcgcccc aagacggaca gggtgacttc tggaagacag tgaagactga      180
aggttttctt ggcttctggg gctcatctgg ctctgattcc ggctccttct ccaggtcaag      240
atccagggtt cagagctact ttcttgggg actactnggg aatcccggtt tcattctgggg      300
gtngaggggg gacggggnaa gggncatgct tgtgaccctt gttcccacc tcggcccgcg      360
accacgctaa ggcccgaatt ncagcacact tggcggcccg t      401

<210> 115
<211> 401
<212> DNA
<213> Homo sapien

<400> 115
atccctgtaa gtctattaaa tggtaataat acataactttt caacttctct tagtcggccc      60
ttggcagatt aaatctttgc aaaattccat atgtgttattt gaaaaatgaa ataaaaccc      120
agatgtctga attcttattt caaatacagt tatataatta ttttaaatta caatatacaa      180
tttctgttaa atacaactgt taagggattt tgagaacaat tataagatta taataatata      240
tacaaaactaa ctctgtaaaat gacatgggtt gtttccttcc caccctccta ccctctcaa      300
gagttttgc atttgctgtt cctgggtgca aaaggcaaaa gaaaatctaa aaatagtctg      360
tgtgtgtcca cgacatgctc gtcctttga gaatctcaa c      401

<210> 116
<211> 301
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

<400> 116
ngatttaatt gnnagttct tttaatgga atnnttggct aaaaatgaatt gatgattatg      60
aatatcccta ggaggagtta gcatggannn tggatcattt cttnnactc ctttangaca      120
nggaaacagg natcagcatg anggtancan aaaccttattt accnangcgc acganctgac      180
ttcttccaaa gagttgnngt tccgggcagc ggtcattgcc gtgcccattt ctggagggt      240
gattcttagtg ntgttattt tgctggccctt gaggatgctt ccaanatgaa aataagangc      300
t      301

<210> 117
<211> 383
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(383)

```

<223> n = A,T,C or G

<400> 117

aattgcaact ggactttat tggcagttt	cnaacaacnaa tgtttcana	aaaatatttg	60
aaaaaaatat accacttcat	agctaagtct tacagagaan	aggatttgct	120
aagtttgaa aattaagatg	cnggtanagc ttctgaacta	atgcccacag ctccaaggaa	180
nacatgtcct atttagttat	tcaaataccca gttgagggca	tttgattaa gcaaacaata	240
tatTTgttan aactttgntt	ttaaattact gntncttgac	attacttata aaggagnctc	300
taactttcga tttctaaaac	tatgtaatac aaaagtatan	ntttccccat tttgataaaa	360
gggcnanga tactgantag	gaa		383

<210> 118
<211> 301
<212> DNA
<213> Homo sapien

<400> 118

ctgctagaat cactgccgt gtgcttcgt	ggaaatgaca gttccttgg	tttttgg	60	
ctgttttgtt tttacattag tcattggacc	acagccattc aggaactacc	ccctgcccc	120	
caaagaaatg aacagttgt	gggagaccca gcagcacctt	tcctccacac accttcattt	180	
tgaagttcg	gttttgg	taagtttaatc tgtacattct	gtttgccatt gttacttgta	240
ctatacatct	gtatatagtg tacggcaaaa	gagtattat ccactatctc tagtgcttga	300	
c			301	

<210> 119
<211> 401
<212> DNA
<213> Homo sapien

<400> 119

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tacaacacag gaaactgttgg	tttacatcg	cgcttgg	120
acgagacgg gctgcgtt	tgtgtgaat	ggggaggaaa	180
aacaagctt	tgggtataaa	agactttac	240
gatgcttaag tgcattggac	agtaaatgaa	tttgaactt atgttgagg	300
gggttgaaa atataaactg	ctttgagca	gtttaagtca	360
ggaactttct	ttcagttt	aaaactctc	401
t			

<210> 120
<211> 301
<212> DNA
<213> Homo sapien

<400> 120

tccagagata ccacagtcaa acctggagcc	aaaaaggaca caaaggactc	tcgacccaa	60
ctgccccaga ccctctccag	aggttgggt	gaccaactca	120
gaagctctat ataaatccaa	gacaagcaac	aaacccttga	180
gagtggccac acagtcaagc	tttaaagaaa	tgattattca	240
ttggcagagc agtttgtcct	cctcaatctg	tcacttgggt	300
c	gtttagaaa	caactgacaa	301

<210> 121
<211> 2691
<212> DNA
<213> Homo sapien

<400> 121

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<210> 122

<211> 683

<212> PRT

<213> Homo sapien

<400> 122

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Val	Leu	Gln	His	Ser	Arg	Leu	Arg	Gly	Arg	Gln	His	Gly	Pro	Asn	Val	
				35				40							45	
Cys	Ala	Val	Gln	Lys	Val	Ile	Gly	Thr	Asn	Arg	Lys	Tyr	Phe	Thr	Asn	
				50				55							60	
Cys	Lys	Gln	Trp	Tyr	Gln	Arg	Lys	Ile	Cys	Gly	Lys	Ser	Thr	Val	Ile	
				65				70							80	
Ser	Tyr	Glu	Cys	Cys	Pro	Gly	Tyr	Glu	Lys	Val	Pro	Gly	Glu	Lys	Gly	
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Cys	Pro	Ala	Ala	Leu	Pro	Leu	Ser	Asn	Leu	Tyr	Glu	Thr	Leu	Gly	Val	
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Val	Gly	Ser	Thr	Thr	Thr	Gln	Leu	Tyr	Thr	Asp	Arg	Thr	Glu	Lys	Leu	
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Arg	Pro	Glu	Met	Glu	Gly	Pro	Gly	Ser	Phe	Thr	Ile	Phe	Ala	Pro	Ser	
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Asn	Glu	Ala	Trp	Ala	Ser	Leu	Pro	Ala	Glu	Val	Leu	Asp	Ser	Leu	Val	
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Ser	Asn	Val	Asn	Ile	Glu	Leu	Leu	Asn	Ala	Leu	Arg	Tyr	His	Met	Val	
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Gly	Arg	Arg	Val	Leu	Thr	Asp	Glu	Leu	Lys	His	Gly	Met	Thr	Leu	Thr	
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Ser	Met	Tyr	Gln	Asn	Ser	Asn	Ile	Gln	Ile	His	His	Tyr	Pro	Asn	Gly	
				195				200							205	
Ile	Val	Thr	Val	Asn	Cys	Ala	Arg	Leu	Leu	Lys	Ala	Asp	His	His	Ala	
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Thr	Asn	Gly	Val	Val	His	Leu	Ile	Asp	Lys	Val	Ile	Ser	Thr	Ile	Thr	
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Asn	Asn	Ile	Gln	Gln	Ile	Ile	Glu	Ile	Glu	Asp	Thr	Phe	Glu	Thr	Leu	
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Arg	Ala	Ala	Val	Ala	Ala	Ser	Gly	Leu	Asn	Thr	Met	Leu	Glu	Gly	Asn	
				260				265							270	
Gly	Gln	Tyr	Thr	Leu	Leu	Ala	Pro	Thr	Asn	Glu	Ala	Phe	Glu	Lys	Ile	
				275				280							285	
Pro	Ser	Glu	Thr	Leu	Asn	Arg	Ile	Leu	Gly	Asp	Pro	Glu	Ala	Leu	Arg	
				290				295							300	
Asp	Leu	Leu	Asn	Asn	His	Ile	Leu	Lys	Ser	Ala	Met	Cys	Ala	Glu	Ala	
				305				310							320	
Ile	Val	Ala	Gly	Leu	Ser	Val	Glu	Thr	Leu	Glu	Gly	Thr	Thr	Leu	Glu	
				325				330							335	
Val	Gly	Cys	Ser	Gly	Asp	Met	Leu	Thr	Ile	Asn	Gly	Lys	Ala	Ile	Ile	
				340				345							350	
Ser	Asn	Lys	Asp	Ile	Leu	Ala	Thr	Asn	Gly	Val	Ile	His	Tyr	Ile	Asp	
				355				360							365	
Glu	Leu	Leu	Ile	Pro	Asp	Ser	Ala	Lys	Thr	Leu	Phe	Glu	Leu	Ala	Ala	
				370				375							380	
Glu	Ser	Asp	Val	Ser	Thr	Ala	Ile	Asp	Leu	Phe	Arg	Gln	Ala	Gly	Leu	
				385				390							400	
Gly	Asn	His	Leu	Leu	Ser	Gly	Ser	Glu	Arg	Leu	Thr	Leu	Leu	Ala	Pro	Leu
				405				410							415	
Asn	Ser	Val	Phe	Lys	Asp	Gly	Thr	Pro	Pro	Ile	Asp	Ala	His	Thr	Arg	
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Asn	Leu	Leu	Arg	Asn	His	Ile	Ile	Lys	Asp	Gln	Leu	Ala	Ser	Lys	Tyr	
				435				440							445	

Leu Tyr His Gly Gln Thr Leu Glu Thr Leu Gly Gly Lys Lys Leu Arg
 450 455 460
 Val Phe Val Tyr Arg Asn Ser Leu Cys Ile Glu Asn Ser Cys Ile Ala
 465 470 475 480
 Ala His Asp Lys Arg Gly Arg Tyr Gly Thr Leu Phe Thr Met Asp Arg
 485 490 495
 Val Leu Thr Pro Pro Met Gly Thr Val Met Asp Val Leu Lys Gly Asp
 500 505 510
 Asn Arg Phe Ser Met Leu Val Ala Ala Ile Gln Ser Ala Gly Leu Thr
 515 520 525
 Glu Thr Leu Asn Arg Glu Gly Val Tyr Thr Val Phe Ala Pro Thr Asn
 530 535 540
 Glu Ala Phe Arg Ala Leu Pro Pro Arg Glu Arg Ser Arg Leu Leu Gly
 545 550 555 560
 Asp Ala Lys Glu Leu Ala Asn Ile Leu Lys Tyr His Ile Gly Asp Glu
 565 570 575
 Ile Leu Val Ser Gly Gly Ile Gly Ala Leu Val Arg Leu Lys Ser Leu
 580 585 590
 Gln Gly Asp Lys Leu Glu Val Ser Leu Lys Asn Asn Val Val Ser Val
 595 600 605
 Asn Lys Glu Pro Val Ala Glu Pro Asp Ile Met Ala Thr Asn Gly Val
 610 615 620
 Val His Val Ile Thr Asn Val Leu Gln Pro Pro Ala Asn Arg Pro Gln
 625 630 635 640
 Glu Arg Gly Asp Glu Leu Ala Asp Ser Ala Leu Glu Ile Phe Lys Gln
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 Ala Ser Ala Phe Ser Arg Ala Ser Gln Arg Ser Val Arg Leu Ala Pro
 660 665 670
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<210> 123
 <211> 1205
 <212> DNA
 <213> Homo sapien

<400> 123

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<210> 130

<211> 1274

<212> DNA

<213> Homo sapien

<400> 130

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<210> 131

<211> 554

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (554)

<223> n = A,T,C or G

<400> 131

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<210> 132
<211> 787
<212> DNA
<213> Homo sapien

<400> 132						
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<210> 133
<211> 219
<212> DNA
<213> Homo sapien

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<223>	n = A,T,C or G					
<400> 133						
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<210> 134
<211> 234
<212> DNA
<213> Homo sapien

<400> 134						
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ttagtaatttca	acattta	acgttagcgc	ttgctgaat	acgccttgc	taaaaaagag	180
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<210> 135

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<211> 414
<212> DNA
<213> Homo sapien

<400> 135
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<210> 136
<211> 461
<212> DNA
<213> Homo sapien

<400> 136
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agactcctataaatcagca cagttcaaaa cttcacctgc ctcaagccaa cagctcattt 180
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gaagtagttc tggccaggcttgcaatacacacaacacaag a 461

<210> 137
<211> 269
<212> DNA
<213> Homo sapien

<400> 137
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ataggttgt tagtttaca tcataatattt gtaatagtgaa aacctgtact caaaatataa 120
gcagcttcaa actggcttta ccaatcttga aatttgcacca caagtgtctt atatatgcag 180
atctaataatgtaaatccagaa cttggactcc atcgtttaaaa ttatttatgt gtaacattca 240
aatgtgtca ttaaatatgtcttccacagttt 269

<210> 138
<211> 452
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(452)
<223> n = A,T,C or G

<400> 138
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tttcatgtgc caatctggaa aaaaataatt taaatcaaca gaacagacag tacatctaca 180
caaatgagga aagcagaaaa gatacctcac attcatttat ctcaggttcaaaatggctt 240

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caatgctaaa gtaaatgtat taacatttgg aaaataacaag acaattttt tgggggtttt	300
caatttttt agctctatac aatgattaca acataagaca aaaaaaaaaaa aaaaacacaa	360
aaaacaaaaac aaaaaaggag ttccaggactt gttatcgttgc tccaaatggc taanaactgg	420
ttcccataac aagcattgaa agttaaggcc cc	452

<210> 139
<211> 474
<212> DNA
<213> Homo sapien

<400> 139	
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cattgggttg tttgttgtct ctttgcatta gatatatgtt agtccttgg cataaatttg	180
acattggtag gggactgaca ttctaacctg gcccaggccc taggagagag ataactccac	240
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gagaatcaac ctcaagcacaa acgcagggtgg ctgggctctg ttccccctta gccaccaccc	420
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<210> 140
<211> 487
<212> DNA
<213> Homo sapien

<400> 140	
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cagcatccag actttcagga agggcagggc cagccagtcc agaaccgcattt ccctcagcag	420
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ctgggggg	487

<210> 141
<211> 248
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (248)
<223> n = A,T,C or G

<400> 141	
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agagattgtc ctgcaacaat attatgttta gtttactgc agaatgataa ctggatcttca	180
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agctaattt	248

<210> 142
<211> 173

<212> DNA
<213> Homo sapien

<400> 142

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attnaagtct agaaagaatc taaaaggctc atcttatagt aaccagaggc agg	173

<210> 143
<211> 511
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (511)
<223> n = A,T,C or G

<400> 143

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ttcagggcag agggaatgag gcaacccagt ggcagccccg ctgggccccg tggctcctgc	120
tctccttattg gacgttagagg caggggagag acttctctat acaaataattc tcacatcacaga	180
agggatgatc cttgctgctc tgccgttaggg tttttagatgc tgagctatgc tgcacatgac	240
gttaacctaa agaacttgga ctgagctttt aaaaaaggac agcaaaacaat ttataatcc	300
ttaaagtgtt atagacgggtt acactagtgc agggattttgg ggaggcttt tgggtgttgg	360
ggctgtcaact tgtatattt gtgactctaa atctttgata gtaaaacaaa tgtaaaaaga	420
aatgtttgcc accagatggg aatagaagtt ccaataagca ggctggaatg ggtggctata	480
cgttgtatca cgaggaagtt ttagactctg a	511

<210> 144
<211> 190
<212> DNA
<213> Homo sapien

<400> 144

cattcttctg tcacatgcca attcagttgt caatcccatt gtctatgctt accggAACCG	60
agacttccgc tacacttttc acaaaattat ctccaggtat cttctctgcc aagcagatgt	120
caagagtggg aatggtcagg ctgggttaca gcctgcttc ggtgtggcc tatgtatctag	180
gctctcgccct	190

<210> 145
<211> 169
<212> DNA
<213> Homo sapien

<400> 145

gatgtggta tctcctcaga tggcagttt gccctctcag gctctggga tggAACCCCTG	60
cgcctctggg atctcacaac gggcaccacc acgaggcgat ttgtggccca taccaaggat	120
tgctgagtg tggccttctc ctctgacaac cgccagattt gctctggat	169

<210> 146
<211> 511
<212> DNA
<213> Homo sapien

<400> 146

atctagagaa	gattggaa	acacatgata	gctatggta	aatacttaac	aggcaatca	60
caggaaagat	gactagatt	cctaacatcc	atgagtgaaa	tttataagaag	tatactct	120
gacttgatat	aaaggaagat	tttaaaaaac	atgactgttc	aggagtgtc	aagttagggc	180
agatgaccag	tgattggaa	tacttcgtaa	gcaggagcaa	gtaagatctg	agccactgtt	240
ctatcggtag	ggtgtctgt	gtattcctt	gtcaaagaag	tactctaagc	aacttcagtc	300
tcacgaatta	ctatcaccc	cgtggcata	catgatggtt	accctaaaga	ggaagttca	360
gaaggcagta	atattggatc	ctggaatagt	cagacaggag	ccttcatgca	gataaccctt	420
tcagttctcc	atacacccat	tcacaagtgg	tcacaaaaac	acccagtacc	tttacttggc	480
tttacccact	taacaatatg	ctcaaatatga	g			511

<210> 147

<211> 421

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (421)

<223> n = A,T,C or G

<400> 147

gaccagtta	gttcttcctg	gctattgtat	aatccacagc	cacactgtga	aagcaaatct	60
ggccagttag	caacacaggg	agaatctgcc	tgaactgacc	aaagggtgtcc	atacttcatg	120
tcagtgagaa	tttcacacct	atcatgttct	aaagagccaa	caacagattc	tagggcactg	180
caaatacgctt	cagaattaa	ttgaaggct	gtttagtac	attcatcatc	tttgagaatg	240
ctttctgggt	cgttgtgagt	cttgtgtct	atatatgcag	ccaaatgagt	ttcagtagacag	300
ccacccccc	acaaagccca	tggttcctt	agtgttaact	gcaggacatg	cagtggcg	360
tgacacgtga	gcttcagtc	atcccangca	gtgtcatttc	tgttgagag	aagccaagct	420
g						421

<210> 148

<211> 237

<212> DNA

<213> Homo sapien

<400> 148

acacaccact	gttggccttc	catctgggtt	aagtcaactg	tgagtagaaa	ccgaagataa	60
cagttttgta	ttcataatgg	cctttcata	ctccaaagtac	ttttgagcac	agagcctt	120
gcttctgacc	tggcacttgg	aacacagata	tatatatctt	ttgttctgtc	cctggaaac	180
tgatatttgt	gtaagacaac	caccagatat	tttctcta	aaaatcttct	aaaatta	237

<210> 149

<211> 168

<212> DNA

<213> Homo sapien

<400> 149

agagaaaagtt	aaagtgaat	aatgttgaa	gacaataagt	ggtggtgtat	tttgcatttct	60
ataagataaa	ctttttgtc	tttgctttat	cttattaggg	agttgtatgt	cagtgtataa	120
aacatactgt	gtggtataac	aggcttaata	aattctttaa	aaggagag		168

<210> 150

<211> 68

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(68)

<223> n = A,T,C or G

<400> 150
 ggtggggtt ggcagagatg anttaagtg ctgtggccag aagcgggggg ggggtttggt 60
 gaaattt 68

<210> 151
 <211> 421
 <212> DNA
 <213> Homo sapien

<400> 151
 aggtgacacg tattcgggat gaaagtataa tagtcattcc ttcaaccctt gcatttatgg 60
 actctggaaa tcgaagatcc acagttagta aagatgttcg tccaaagaca aaaaatagaa 120
 acagctcaac aaagcgagag aaaaaaaaaac aaaatggcac tgtggctctg cctttgaagt 180
 ctgggctcca gcagagggct gatctccca caggagacga gacggcctat gacactctcc 240
 agaactgttg tcagtgccga atttacttc cttgccccat tctaaatgag caccaggaga 300
 agtgcagag gttagctcac caaaagaaac tccagtgggg ctggtagat ggctcagcgg 360
 gtaagagcac ccgactgctc ttccgaaggt ccggagttca aatcccagca accacatgg 420
 g 421

<210> 152
 <211> 507
 <212> DNA
 <213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(507)

<223> n = A,T,C or G

<400> 152
 gaattcggca cnagctcggt ccggcagggt ngtccnttt tttgtccgc ctcgccanga 60
 cttccatcag ctatcgccag tcgtccggca cgtcntccctt cngaggcctg ggcggcgct 120
 ccgtcggttn tggccgggg gtcgccttcc nctcnccctt cattcaegggg ggctccggcg 180
 gcccgccgt atccgtgtcc tccgccccgt ntgtgtccctc gtcctccctcn ggggcctacg 240
 gctngctgct acngcggctt cctgaccgct tccnacgggc tgctggcngg caacgagaag 300
 ctaaccatgc agaacctnaa cnaccgcctg gcttccttacc tgnacaaggt ggcgcncctg 360
 taggcggcca acggcnagct agaggtgaag atccnctact gggtaccaga agcaggggcc 420
 tggccctgc ccgactacag ccactnctnc acnaccatgc agtacctgcn ggganaagat 480
 tntngggngc caccatngag aactgca 507

<210> 153
 <211> 513
 <212> DNA
 <213> Homo sapien

<400> 153
 gaattcggca cgaggtggct cagatgtcca ctactggag tatggtcgaa ttggaaattt 60
 tattgtgaaa aagcccatgg tgctgggaca tgaagctcg ggaacagtcg aaaaagtggg 120

atcatcggtaa	aaccaccta	aaccaggta	tctgttgc	atcgagcctg	gtgcctcccg	180
agaaaaatgt	gaattctgca	agatggccg	atacaatctg	tcaccttcca	tcttcttctg	240
tgccgcgc	cccgtacgt	gaaacotctg	ccggttctat	aagcacaatg	cagcctttg	300
ttacaagctt	cctgacaatg	tcaccttga	ggaaggcgcc	ctgatcgagc	cactttctgt	360
ggggatccat	gcctgcagga	gaggcggagt	taccctggga	cacaaggccc	ttgtgtgtgg	420
agctgggcca	atcgggatgg	tcacttgct	cgtggccaaa	gcaatggag	cagctcaagt	480
agtggtaact	gatctgtctg	ctaccggatt	gtc			513
<210> 154						
<211> 507						
<212> DNA						
<213> Homo sapien						
<220>						
<221> misc_feature						
<222> (1)...(507)						
<223> n = A,T,C or G						
<400> 154						
ggcacgagct	cgtgccgaat	tcggcnccgag	cagacacaat	ggtaagaatg	gtgcctgtcc	60
tgctgtctct	gctgctgctt	ctgggtcctg	ctgtccccca	ggagaaccaa	gatggtcgtt	120
actctctgac	ctatatctac	actggctgt	ccaaagcatgt	tgaagacgtc	ccgcgcgtttc	180
aggcccttgg	ctcactcaat	gacctccagt	tctttagata	caacagtaaa	gacaggaagt	240
ctcagcccat	gggactctgg	agacaggtgg	aaggaatgga	ggatttggaaag	caggacagcc	300
aacctcagaa	ggccaggggag	gacatctta	tggagacccct	gaaagacatc	gtggagtatt	360
acaacgcacag	taacgggtct	cacgtattgc	agggaaagtt	tggttgtgag	atcgagaata	420
acagaagcag	cggagcattc	tggaaatatt	actatgtgg	aaaggactac	attgaattca	480
acaaaagaaat	cccagcctgg	gtccccct				507
<210> 155						
<211> 507						
<212> DNA						
<213> Homo sapien						
<220>						
<221> misc_feature						
<222> (1)...(507)						
<223> n = A,T,C or G						
<400> 155						
ggcacgagga	gacctaagggt	ctgagtnctg	ggaacaggag	aaagctctgt	tggccctcca	60
gcagcagtgt	gctgagcagg	cacaggagca	tgaggtggag	accaggccc	tgcaggacag	120
ctggctgcag	gccaggcag	tgctcaagga	acgggaccag	gagcttggaaag	ctctgcgggc	180
agaaaagtca	tcctcccgcc	atcaggagga	ggctgcccgg	gcccgggctg	aggctctgca	240
ggaggccctt	ggcaaggctc	atgctccct	gcaggggaaa	gagcagcatc	tcctcgagca	300
ggcagaattg	aqccgcagtc	tggaggccag	cactgcaacc	ctgcaaggct	ccctggatgc	360
ctgccaggca	cacagtccgc	agctggagga	ggctctgagg	atacaagaag	gtgagatcca	420
ggaccagat	ctccgataacc	aggaggatgt	gcagcagctg	cagcaggcac	ttgcccagag	480
ggatgaagag	ctgagacatc	agcagga				507
<210> 156						
<211> 509						
<212> DNA						
<213> Homo sapien						

<220>
 <221> misc_feature
 <222> (1)...(509)
 <223> n = A,T,C or G

<400> 156

ggcacgagga cagagagaac	cctgtngaaa gagcgttacc	aggaggcct ggacaaacag	60
aggcaagtgg agaatcagct	ccaagtgc当地 ttaaaggcagc	ttagcacaag gagagaagag	120
gaaatgaaga atcaccagga	gatattaaag gctattcagg	atgtgacaat aaagcgggaa	180
gaaacaaaga agaagataga	gaaagagaag aaggagttt	tgcagaagga gcaggatctg	240
aaagctgaaa ttgagaagct	ttgtgagaag ggcagaagag	aggtgtggga aatggaaactg	300
gataactca agaatcagga	tggc当地ata aataggaaca	ttatgaaaga gactgaacgg	360
gcctt当地agg cagagatctt	atcaactagag agccggaaag	agttactggt actgaaacta	420
gaagaagcag aaaaagagc	agaattgcac ctacttacc	tcaagtcaac tcccccaaca	480
ctggagacag ttcttccaa	acaggagtg		509

<210> 157
 <211> 507
 <212> DNA
 <213> Homo sapien

<400> 157

ggcacgaggg cagccctcct	accggcgcac gtgggtccgc	cgctgtgcc tcccgtcgc	60
cctgaaccca gtgc当地cg	ccatggctcc cggccagctc	gccttattta gtgtctctga	120
caaaaccggc ct当地ggaa	c当地gaccgct cttgggta	atctggctgc	180
ttccggaggg actgcaaag	ctctcaggga tgctggctg	gcagtcagag atgtctctga	240
gtt当地ggaa tt当地ctgaa	tttgggggg acgtgtgaa	acttgc当地 ctgc当地cca	300
tgctgaaatc ct当地cgta	atattccaga agataatgct	gacatggcca gacttgatt	360
caatcttata agagtttgg	c当地caatct ctatccctt	gtaaagacag tggcttctcc	420
aggtgtaagt gttgaggagg	ctgtggagca aattgacatt	ggtggagtaa cttactgag	480
agctgcagcc aaaaaccacg	ctcgag		507

<210> 158
 <211> 507
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(507)
 <223> n = A,T,C or G

<400> 158

ggcacgagtc gagctgtgcc	tattcngtc aatccaagag	tgagtaatgt gaagtctgtc	60
tacaaaaccc acattgatgt	cattcattat cggaaaacgg	atgcaaaacg tctgc当地ggc	120
ctt当地atgaaag aagcagaaca	gaaactttt tc当地gaaac	gtgtgaaatt gcttaaggaa	180
ctt当地ccagga aaccagacat	ttatgagagg cttgcttcag	c当地ggctcc aagcatttat	240
gaacatgaaag atataaagaa	ggaaattttg cttcagctct	ttggc当地ggac aaggaaggat	300
tttagtc当地a ct当地ggagg	caaatttc当地g gctgagatca	acatottgct gtgtggc当地g	360
c当地ggtacca gcaagtc当地ca	gctgctgc当地g tacgtgtaca	acctc当地gccc cagggccag	420
tacacgtna ggaagggctc	c当地gtcannt ggc当地nactg	cntacgtaat gaaagaccct	480
gagacaaggn anctggnnc	gnnacag		507

<210> 159
 <211> 508

<212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(508)
 <223> n = A,T,C or G

<400> 159

ggcacnanaa accaggatta tggtnnggat ccaaagattg ctaatgcaat aatgaaggca 60
 gcagatgagg tagctgaagg taaattaaat gatcatttc ctctcggtt atggcagact 120
 ggt:caggaa ctcagacaaa tatgaatgt aatgaagtca ttagcaataag agcaattgaa 180
 atgttaggag gtgaacttgg cagcaagata cctgtgcatt ccaacgatca tgttaataaa 240
 agccagagct caaatgatac tttcccaca gcaatgcaca ttgctgctgc aatagaagtt 300
 catgaagttac tggtaaccagg actacagaag ttacatgatg ctcttgatgc aaaatccaaa 360
 gagttgcac agatcatcaa gattggacgt actcatactc aggatgctgt tccacttact 420
 cttgggcagg aatttagtgg ttatgttcaa caagtaaaat atgcaatgac aagaataaaa 480
 gctgccatgc caagaatcta tgagctcg 508

<210> 160
 <211> 508
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(508)
 <223> n = A,T,C or G

<400> 160

ggcacgagct tggagcaaag tcatctnaag gaatttagagg acacacttca ggtaggcac 60
 atacaagagt ttgagaaggt tatgacagac cacagagttt ctttgagga attaaaaaag 120
 gaaaaccaac aaataattaa tcaaatacaa gaatctcatg ctgaaattat ccaggaaaaa 180
 gaaaaacagt tacaggaatt aaaactcaag gtttctgatt tgtcagacac gagatgcaag 240
 ttagaggttgcgtt gaaggaagca gaaactgtatg aaataaaaat ttgctggaa 300
 gaaagcagag cccagcagaa ggagacctt 66 aaatctttc ttgaacaaga gacagaaaat 360
 ttgagaacag aaatttagtaa actcaaccaa aagattcagg ataataatga aaattatcag 420
 gtggccttag cagagctaag aactttaatg acaattgaaa aagatcagtg tatttccgag 480
 ttaatttagta gacatgaaga agaatcta 508

<210> 161
 <211> 507
 <212> DNA
 <213> Homo sapien

<400> 161

ggcacgagcg ctaccggcgc ctctctgctg gccactgagc cggagccggc ctgagcagcg 60
 ctctcggtt cagtagccac tggaaaggact taggcgctcg cgtggacacc gcaagcccc 120
 cagtagcctc ggcccaagag gcctgtttc cactcgctag ccccccggg ggtccgtgtc 180
 ctgtctcggtt ggccggaccc gggcccggc ccgagcagta gcccggccca tgcgtgtgt 240
 gggcatagac ctggccttcc agagctgta cgtcgctgt gcccggcccg gccgcattcga 300
 gactatcgct aatgagtata gcgaccgctg cacgcccggct tgcatttctt ttggctctaa 360
 gaatcggtca attggagcag cagctaaaag ccaggttaatt tctaattgcaaa agaacacagt 420
 ccaaggattt aaaagattcc atggccggc attctctgtat ccatttgcgg aggccagaaaa 480
 atctaacctt gcatatgata ttgtgca 507

<210> 162
 <211> 507
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (507)
 <223> n = A,T,C or G

<400> 162

ggcacgagca	gctgtgcacc	gacatgntct	cagtgtcctg	agtaagacca	aagaagctgg	60
caagatcctc	tctaataatc	ccagcaaggg	actggccctg	ggaattgcca	aagcctggga	120
gctctacggc	tcacccaatg	ctctggtgct	actgattgct	caagagaagg	aaagaaaacat	180
atttgaccag	cgtgccatag	agaatgagct	actggccagg	aacatccatg	tgatccgacg	240
aacatttcaa	gatatctctg	aaaaggggtc	tctggaccaa	gaccgaaggc	tgttgtgga	300
tggccagggaa	attgctgtgg	tttacttccg	gatggctac	atgcctcgtc	agtagtct	360
acagaatttgg	gaagcacgtc	tactgctgga	gaggtcacat	gctgccaagt	gcccgacat	420
tgccacccag	ctggctggga	ctaagaaggt	gcagcaggag	ctaagcaggc	cgggcatgct	480
ggagatgttg	ctccctggcc	agcctga				507

<210> 163
 <211> 460
 <212> DNA
 <213> Homo sapien

<400> 163

ggcacgagaa	ataactttat	ttcattgtgg	gtcgcggttc	ttgtttgtgg	atcgctgtga	60
tcgtcaactg	acaatgcaga	tcttcgtgaa	gactctgact	ggtaagacca	tcaccctcga	120
ggttgagccc	agtgcacacca	tcgagaatgt	caaggcaaag	atccaagata	aggaaggcat	180
ccctctgac	cagcagaggc	tgatcttgc	tggaaaacag	ctgaaagatg	ggcgccacct	240
gtctgactac	aacatccaga	aagagtccac	cctgcacctg	gtgctccgtc	tcagagggtgg	300
gatgcaaatac	ttcgtgaaga	cactcaactgg	caagaccatc	acccttgagg	tggagcccg	360
tgacaccatc	gagaacgtca	aagcaaagat	ccaggacaag	gaaggcattc	ctcctgacca	420
gcagagggtt	atctttgcgg	gaaagcagct	ggaagatggg			460

<210> 164
 <211> 462
 <212> DNA
 <213> Homo sapien

<400> 164

ggcacgagcc	ggatctcatt	gccacgcgcc	cccgacgacc	gcccacgtg	cattcccgat	60
tcctttgggt	tccaagtcca	atatggcaac	tctaaaggat	cagctgattt	ataatcttct	120
aaaggaagaa	cagaccccccc	agaataagat	tacagttgtt	ggggttggtg	ctgttgcac	180
ggcctgtgcc	atcgttatct	taatgaagga	cttggcagat	gaacttgctc	ttgttgatgt	240
catcgaagac	aaattgaagg	gagagatgt	ggatctccaa	catggcagcc	ttttcccttag	300
aacaccaaag	attgtctctg	gcaaagacta	taatgttaact	gcaaactcca	agctggcat	360
tatcacggct	ggggcacgtc	agcaagaggg	agaaagccgt	cttaatttgg	tccagcgtaa	420
cgtgaacatc	tttaaattca	tcattcctaa	tgttgtaaaa	ta		462

<210> 165
 <211> 462
 <212> DNA

<213> Homo sapien

<400> 165

ggcacgagga agccatgagc agcaaagtct ctcgcacac cctgtacgag gcggtgcggg	60
aagtccctgca cgggaaccag cgcaagcgcc gcaagttcct ggagacggtg gagttgcaga	120
ttagcttcaa gaactatgtat ccccagaagg acaagcgctt ctcggcacc gtcaggctta	180
agtccactcc cccgcctaag ttctctgtgt gtgtcctggg ggaccagcag cactgtgacg	240
aggctaaggc cgtggatatac ccccacatgg acatcgagggc gctaaaaaaa ctcacaaga	300
ataaaaaact ggtcaagaag ctggccaaga agtatgatgc gttttggcc tcagagtctc	360
tgtatcaagca gattccacga atcctcggcc caggttaaa taaggcagga aagttccctt	420
ccctgctcac acacaacgaa aacatggtgg cccaaagtgg tg	462

<210> 166

<211> 459

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(459)

<223> n = A,T,C or G

<400> 166

ggcacgagag ggacctgtnt gaatggntcc actagggttn anntgnctct tacttttaac	60
cantnaaatn gacctgcccc tgaanangcg ggcntgacac annaanacga gaagacccta	120
tggagctta atttattaat gcanacagna cctaacaac ccacangtcc taaactacca	180
agcctgcatt aaaaatttcg gntggggcna cctcnagca naacccaacc tccgagcaac	240
tcatgctaag acttcaccag tcaaagctga actactatac tcaattgatc caataacttg	300
accaacagan caagntaccc tagggataac ancacaatcc tattctagac cccttatnac	360
caatangntt tacacctcna tnnggaacc aggacatccg atggggcagn cgttattaaa	420
gttngttgnt aacnataaaag tctacgtat ctgagttag	459

<210> 167

<211> 464

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(464)

<223> n = A,T,C or G

<400> 167

gaattgggac caacganaan cngcggntc ttntttgcn tccanngccc agctnattgc	60
tcagacacac atggggaaagg tnaaggctgg gagtcaacng atttggtngt attgnagcgt	120
ttggtcacca gngctgctt taactctggn aaagtggata ttgttgtcat naatgacccc	180
tncattgacc tnaactacat ggtttacatg ttccaatatg attccaccca tggcaaattc	240
catngcaccg tnaaggctga gaacggaaag cttgtnatca atggaaatcc catcaccatc	300
tttcangaac ganatccntn caaaaatcaa anttgggggc gatgcttggc cncttgaagt	360
accgttcaan gggaaannnc ccactttggc cgntntttnc aancccaccc caatttgggn	420
aaaaaaaaaaag gggnnnttgg gggggggcct tttanntttt tttt	464

<210> 168

<211> 462

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(462)

<223> n = A,T,C or G

<400> 168

ggcacgaggn nnaacctncg gggctgggc agcacgcctt gngcaancct gcactgcact	60
gaagacccgg tgccggaagc cgnngcngc nacatgcagn aactgaacca gctggcgcg	120
cancagttct cagacctgac agaggtgctt ttacacttcc taactgatcc anantangtg	180
gaaatattnt tngtnatnt catntgaatn atccancncc aatcatanca nttnattn	240
cctcataaanc ntgagaana gcnnccntnt gntncanan ggtgctntga anangagtct	300
cacangcaan caggtccaag cggtttnnt aactntgggt ctatgang agaaagnac	360
ttactttctt gaaancngga agcagaatgc tcccaccctt gctcgatggg ccatacgtca	420
agactctgat gattaaccag cttnatata ggacnggaaa tt	462

<210> 169

<211> 460

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(460)

<223> n = A,T,C or G

<400> 169

ggcacgaggg acagcagacn agacagtcac agcagccttg acaaaacgtt cctggaactc	60
aagntctnt ncncaaagga ggacagagca nacagcagag accatggant ctnctcggc	120
ccctccccac agatggtgc tcccctggca naggctctg ctcacagcct cacttctaac	180
cttctggaac cogcccccca ctgccaagct cactattgaa tccacgcccgt tcaatgnntc	240
ntagggaaag gagggcctt ctactntnc acaatctgan ccccttcttn tttggttact	300
ancatggctc tncatgtnaa aatactggna tggntaacct gtcaaattta taggnantnt	360
gctaattggg aaactnccnn tngtctaccc caggggnccc agattcctnn gttcncataa	420
cnattaattt aaccctaat gncaancct tngttaaaga	460

<210> 170

<211> 508

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(508)

<223> n = A,T,C or G

<400> 170

ggcacgaggg ggatttttag gtggtcnggt gtggtatcag gaataatgtg ggaggccaga	60
ttgaagtcca ggccaggaac aatggtaatt gtgggactta agaaagtgtg agtacagctg	120
aatgagccgg ggagcagaaaa gtatatgcgt caggtatgag gaagaaaata gattttggaa	180
gttatagagaa atgttagagag tgagttgagc atagtttgatg attttgaggg cctctaacag	240
tattaaagca gcggcagcgg ctgcacacag acatgtatggc taggctaaaa caggaaggtc	300
aagttgtttg gacagaaaagg ctacagggtg cagtcctggc tcttgtgtaa gaattctgac	360
cacactaacc atgccttagga aggaaaggag ttgttcttt gtaaggatt gaggtttggg	420

agattaatcg gacacgatca gcagggagag cacctgttt tttatgagaa ttatgcttag	480
ataggtaaca gatgaggatg aaatttgg	508
<210> 171	
<211> 507	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1) ... (507)	
<223> n = A,T,C or G	
<400> 171	
ggcacgagac cagccactag cgcnctcg agcgatggcc tatgtccccg caccggcta	60
ccagcccacc tacaacccga cgctgcctta ctaccagccc atcccggcgc ggctcaacgt	120
ggaatgtct gttacatcc aaggagtggc cagcgagcac atgaagcggt tcttcgtgaa	180
cttgggtt gggcaggatc cgggctcaga cgtcgcccttc cacttcaatc cgcggtttga	240
cggctggac aagggtgtct tcaacacgtt gcagggcggg aagtgggca gcgaggagag	300
gaagaggagc atgcccttca aaaagggtgc cgccttgag ctggtcttca tagtcctggc	360
ttagcactac aagggtggtgg taaatggaaa tcccttctat gagtacggc accggcttcc	420
cctacagatg gtcacccacc tgcaagtgg a tgggatctg caacttcaat caatcaactt	480
catcgaggc cagccctcc ggccccca	507
<210> 172	
<211> 409	
<212> DNA	
<213> Homo sapien	
<400> 172	
ggcacgagct ggagtgtctg ctgccacccc ctcgtcctct gcagaaatgt ctgtcaccta	60
cgatgactct gtgggagtgg aagtgtccag cgacagcttc tgggagggttg ggaactacaa	120
acggactgtg aaggcgattt acgtggcca ccgcctgtgt ggtgacctca tgaactgtct	180
gcatgagcgg gcacgcattcg agaaggcgta tgacacagca ctcactgagt gggcccgacg	240
ctggaggcag ctggtagaga agggaccaca gtatggacc gtggagaagg octggatagc	300
tgtcatgtct gaagcagaga gggtagtga actgcacctg gaagtgaagg catcaactgat	360
gaatgaagac ttggagaaga tcaagaactg gcagaaggaa gccttcac	409
<210> 173	
<211> 409	
<212> DNA	
<213> Homo sapien	
<400> 173	
ggcacgaggc cagctagagg aagagtccaa ggccaagaac gcactggccc acgcccctgca	60
gtcagctcg catgactgtg acctgctgca ggaacagtat gaagaggagc aggaagccaa	120
ggctgagctg cagagggcca tgtccaaggc caacagcgag gtagccagt ggaggacgaa	180
atatgagacg gatgccatcc agcgacacaga ggagctggaa gaggccaaga agaagctggc	240
tcagcgctg cagatgtcg aggaacatgt agaagctgtg aattccaaat gcgttctct	300
tgaaaagacg aagcagcgac ttcagaatga agtggaggac ctcatgattg acgtggagag	360
gtctaatgct gcctgcgctg cgcttgataa gaagcagaggaa aactttgac	409
<210> 174	
<211> 407	
<212> DNA	

<213> Homo sapien

<400> 174

ggcacgagcc	ggggcgcccc	gcggcgctcc	ggctcgaggc	attcggagct	gcgggagccg	60
ggctggcagg	agcaggatgg	cgccggcgcc	ggctgcaggc	gaggcgcgcc	gggtgcttgt	120
gtacggcgcc	aggggcccctc	tgggttctcg	atgcgtgcag	gctttcggg	cccgcaactg	180
gtgggttgcc	agcgttcatg	tggtggagaa	tgaagaggcc	agcgctagca	tcattgttaa	240
aatgacagac	tcgttcaactg	agcaggctga	ccaggtgact	gctgagggtt	gaaagcttt	300
gggtgaagag	aagggtggat	caattcttg	cgtgctgga	ggatggccg	ggggcaatgc	360
caaataccaag	tctctttta	agaactgtga	cctgatgtgg	aagcaga		407

<210> 175

<211> 407

<212> DNA

<213> Homo sapien

<400> 175

ggcacgagct	tgcggcgtcg	tcgcttagctc	gctcggtgcg	cgtcgcccc	ctccatggcg	60
ctcttcgtgc	ggctgctggc	tctcgccctg	gctctggccc	tgggccccgc	cgcgaccctg	120
gcgggtcccc	ccaaagtgcgc	ctaccagctg	gtgctgcagc	acagcaggct	ccggggccgc	180
cagcacggcc	ccaaacgtgtg	tgctgtgcag	aaggttattt	gcaactaatag	gaagtacttc	240
accaactgca	acagagtggta	ccaaaggaaa	atctgtggca	aatcaacagt	catcagctac	300
gagtgctgtc	ctggatatga	aaaggtccct	ggggagaagg	gctgtccagc	agccctacca	360
ctctcaaacc	tttacgagac	cctggagtc	gttggatcca	ccaccac		407

<210> 176

<211> 409

<212> DNA

<213> Homo sapien

<400> 176

ggcacgagt	gtgcacaaac	gggaccatgc	cctcctggag	gagcagagca	agcagcagtc	60
caacgacac	ctgcgcgcgc	agttcgcag	ccaggccaaat	gttgtgggc	cctggatcca	120
gaccaagatg	gaggagatcg	ggcgcatctc	cattgagatg	aacgggaccc	tggaggacca	180
gctgagccac	ctgaagcagt	atgaacgcag	catcgtggac	tacaagccca	acctggacct	240
gctggagcag	cagcaccaggc	tcatccagga	ggccctcatac	ttcgacaaca	agcacaccaa	300
ctataccatg	gagcacatcc	gctgtggctg	ggagcagctg	ctcaccacca	ttgcccgcac	360
catcaacgag	gtggagaacc	agatcctcac	ccgcgacgccc	aaggcatac		409

<210> 177

<211> 408

<212> DNA

<213> Homo sapien

<400> 177

ggcacgaggt	ccaggttaact	gcaaaaacaa	tggctcagca	tgaagaactg	atgaagaaaa	60
ctgaaacaaat	aatgttagtt	atggagacca	ataaaatgt	aagagaagag	aaggagcagg	120
tttcaaaaat	ggcatcagtc	cgtcagcatt	tggaaagaaac	aacacagaaa	gcagaatcac	180
agttgttgg	gtgtaaagca	tcttggagg	aaagagagag	aatgttaaag	gatgaagtt	240
ccaaatgtgt	atgtcgctgt	gaagatctgg	agaaacaaaa	cagattactt	catgatcaga	300
tcgaaaaatt	aagtgacaag	gtcgtgcct	ctgtgaagga	aggtgtacaa	ggtccactga	360
atgtatctct	cagtgaagaa	ggaaaatctc	aagaacaaat	tttgaaaa		408

<210> 178

<211> 92

<212> DNA
 <213> Homo sapien

<400> 178
 ggcacgagaa gaaattaaga gctaaagaca aggagaatga aaatatggtt gcaaagctga 60
 acaaaaaagt taaagagcta gaagaggaga tg 92

<210> 179
 <211> 411
 <212> DNA
 <213> Homo sapien

<400> 179
 ggcacgagga gacacgccac ctataccaca gttctcagaa tgaatttagct aagttggaat 60
 cagaacttaa gagtctaaa gaccagttga ctgatttaag taactcttta gaaaaatgt 120
 aggaacaaaa aggaaacttg gaaggatca taaggcagca agaggctgat attcaaaatt 180
 ctaagttcag ttatgaacaa ctggagactg atcttcagggc ctccagagaa ctgaccagta 240
 ggctgcatga agaaaataaat atgaaagagc aaaagattat aagctgtct tctggcaagg 300
 aagaggcaat ccaagtagct attgctgaac tgcgtcagca acatgataaa gaaattaaag 360
 agctggaaaa cctgctgtcc caggaggaag aggagaatat tgtttagaa g 411

<210> 180
 <211> 411
 <212> DNA
 <213> Homo sapien

<400> 180
 ggcacgaggt tggcggcggc gggcgagcgg agtttagcagg gctttactgc agagcgccc 60
 gggcactcca gcgaccgtgg ggatcagcgt aggtgagctg tggccctttg cgaggtgctg 120
 cagccatagc tacgtgcgtt cgctacgagg attgagcgtc tccacccatc ttctgtgctt 180
 caccatctac ataatgaatc ccagtatgaa gcagaaaacaa gaagaaaatca aagagaatat 240
 aaagactagt tctgtccaa gaagaactct gaagatgatt cagccttctg catctggatc 300
 tcttggatggc agagaaaaatg agctgtccgc aggcttgc 360
 ccacttaaca tctacaactt ccagccctgg gtttattgtc ccagaatcta g 411

<210> 181
 <211> 411
 <212> DNA
 <213> Homo sapien

<400> 181
 ggcacgagggc gggacagggc gaagcggcct gcgcacacgg agcgcgcgac actgcccgg 60
 agggaccgccc acccttggcc cctcagctgc ccactcgtga ttccagcgg cctccgcgc 120
 cgcacatgc cctcggccac cagccacagc gggagcggca gcaagtgcgc cggaccgcca 180
 ccggccgtcgg ttccctccgg gagtgaggcg gccgcgggag ccggggccgc cgcgcggct 240
 tctcagcacc ccgcacccgg caccggcgct gtccagaccg aggccatgaa gcagatttc 300
 ggggtgatcg acaagaaaact tcggAACCTG gagaagaaaa agggtaagct tgatgattac 360
 caggaacgaa tgaacaaagg ggaaaggctt aatcaagatc agctggatgc c 411

<210> 182
 <211> 411
 <212> DNA
 <213> Homo sapien

<400> 182

ggcacgagcc gacatggagc tggcttcgc gggccgcgg gtgttgtca ccggggcagg	60
caaaggata gggcgccga cggtccaggc gctgcacgcg acgggcgcg gggtgtggc	120
tgtgagccgg actcaggcgg atcttgcac agtggccgg cttgtccgc gagtgcccgg gatatagaacc	180
cgtgtgcgtg gacctgggtg actgggaggc caccgagcgg ggcgtggca gcgtgggccc	240
cgtggacctg ctggtaaca acggccgtgt cgccctgtg cagcccttcc tggaggtcac	300
caaggaggcc tttgacagat ccttgggtt gaacctgcgt ggcgtcatcc aggtgtcgca	360
gattgtggcc aggggcttaa tagccccggg agtcccaggc gccatcgta a	411

<210> 183

<211> 409

<212> DNA

<213> Homo sapien

<400> 183

ggcacgagcc tacactctgg ccagagatac cacagtcaaa cctggagcca aaaaggacac	60
aaaggactct cgacccaaac tgccccagac cctctccaga ggttgggtg accaactcat	120
ctggacttag acatatgaag aagctctata taaatccaag acaagcaaca aacccttgat	180
gattattcat cacttggatg agtgcacaca cagtcaagct taaaagaaag tttttgtga	240
aaataaagaa atccagaaat tggcagagca gtttgcctc ctcaatctgg tttatgaaac	300
aactgacaaa caccttctc ctgatggcca gtatgtcccc aggattatgt ttgttgaccc	360
atctctgaca gtttagagccg atatcactgg aagatattca aatcgctc	409

<210> 184

<211> 410

<212> DNA

<213> Homo sapien

<400> 184

ggcacgaggt cattccagca ccaacaggat ccaagccaga ttgattggc tgcattggcc	60
caagcttga ttgccccaaag agaagttca ggacagcaaa gcatggtaga acaaccacca	120
ggaatgtatgc caaatggaca agatatgtct acaatggaaat ctggccaaa caatcatggg	180
aatttccaaag gggattcaaa cttcaacaga atgtggcaac cagaatgggg aatgcacatcg	240
caaccccccac accccccctcc agatcagcca tggatgccac caacaccagg cccaatggac	300
attgttcctc cttctgaaga cagcaacagt caggacagtg gggaaattgc ccctgacaac	360
aggcatatat ttaaccagaa caatcacaac ttgggtggac caccgataaa	410

<210> 185

<211> 411

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (411)

<223> n = A,T,C or G

<400> 185

ggcacgagca cagatgttgtt tttctctgcg cgtgtgcgtt ttccctcctc cccgccttc	60
agggtccacg gccaccatgg cgtatttaggg gcagcagtgc ctgcggcagc attggccttt	120
gcagggcgg cagcagcacc aggctctgca gcggcaaccc ccagcggctt aagccatggc	180
gcttctcacg gcattcagca gcagcgttgc tgtaaccgac aaagacacct tcgaattaag	240
cacattcctc gattccagca aagcaccgca acatgaccga aatgagcttc ctgagcagcg	300
agggttttgtt gggggacttg atgtccccct tcgaccgcgtc gggttttggg gctgaagaaa	360
gcctangtct ctttagatgt tacctggagg tggccaaagca cttcaaacct c	411

<210> 186
 <211> 410
 <212> DNA
 <213> Homo sapien

<400> 186
 ggcacgagct tctagtcccg ccatggccgc tctcacccgg gaccccccagt tccagaagct 60
 gcagcaatgg taccgcgagc accgctccga gctgaacctg cgccgcctct tcgatgc当地
 caaggaccgc ttcaaccact tcagcttgcac cctcaacacc aaccatggc atatcctggt 120
 ggattactcc aagaacctgg tgacggagga cgtatgc当地 atgctggc当地 acttggccaa 180
 gtccaggggc gtggaggccg cccgggagcg gatgttcaat ggtgagaaga tcaactacac 240
 cgagggtcga gccgtgctgc acgtggctct gcggAACCGG tcaaacaacac ccatcctggt 300
 agacggcaag gatgtgatgc cagaggtcaa caaggttctg gacaagatga 360
 410

<210> 187
 <211> 506
 <212> DNA
 <213> Homo sapien

<400> 187
 ctttcgtggc tcactccctt tcctctgctg ccgctcggtc acgcttgc当地 ccgaaggagg 60
 aaacagtgc当地 agacctggag actgcagttc tctatccttc acacagctct ttcaccatgc 120
 ctggatcaact tccttgaat gcagaagctt gctggccaaa agatgtggg当地 attgttgccc 180
 tttagatcta tttccttctt caatatgtt当地 atcaaggc当地 gttggaaaaa tatgtatggt 240
 tagatgtctgg aaagtataacc attggcttgg gc当地aggccaa gatggc当地 tgc当地agata 300
 gagaagatata taactcttctt tgc当地actg tggttc当地aa tcttatggag agaaataacc 360
 tttcctatga ttgc当地tggg cggctggaag ttggaaacaga gacaatcatc gacaatcaa 420
 agtctgtgaa gactaattt当地 atgc当地gtt当地 ttgaagagtc tgg当地ataca gatatagaag 480
 gaatcgacac aactaatgca tgctat 506

<210> 188
 <211> 506
 <212> DNA
 <213> Homo sapien

<400> 188
 gccacagagg cggcggagag atggccctca gc当地gttccc当地 ggctccctac ctgagtc当地 60
 ctgtccctt ttctggact attcaaggag gtctccagga cggacttc当地 atcactgtca 120
 atgggaccgt tctc当地actcc agtggaaacca gtttgc当地t当地 gaactt当地c当地 actggcc当地ca 180
 gtggaaatga cattgc当地tcc cacttcaacc ctc当地gtt当地 agatggaggg tacgtgggt 240
 gcaacacgag gc当地aaacgga agctggggcc cggaggagag gaagacacac atgc当地tcc 300
 agaaggggat gc当地ctt当地gac ctctgcttcc tgg当地c当地agag ctc当地attt当地 aagggtatgg 360
 tgaacgggat cctctt当地gtg cagtaatttcc accgc当地gtcc cttccaccgt gtggacacca 420
 tctccgtcaa tggctctgtg cagctgtcc local catc当地gctt ccagc当地tccc ggc当地gtg当地ggc 480
 ctgccaaccc ggctccctt accccag 506

<210> 189
 <211> 399
 <212> DNA
 <213> Homo sapien

<400> 189
 ctggacagga gaagagcctg gctgctgaag gc当地ggctga cacgaccacg ggc当地gttcc 60
 ctggagcccc agaggatgaa agatcgacaga gc当地agcccc ccaggacca gagtc当地tcc 120
 accctgcccc accggcttggg ctc当地gtgaggc cgacatctgg ctttccc当地 ag gccc当地aggaa 180

aggaaacctt ggaaagtgc ctaatcgctc tagactctga aaaacccaag aaacttcgct	240
tccacccaaa gcagctgtac ttctctgcc a ggcagggtga gctcagaag gtgcattctca	300
tgctgggtga tggatttatccc aatggagca ccaaagtaag cgttccccat	360
tacatgctgc tgccgaggct ggccacgtgg acatctgcc	399

<210> 190
<211> 401
<212> DNA
<213> Homo sapien

<400> 190	
cggcgacggg ggtgggtgact gagcggagcc cggtgacagg atgttgtgt tggtatttagg	60
agatctgcac atccccacacc ggtcaacag tttgcacact aaattcaaaa aactcctgg	120
gccaggaaaa attcagcaca ttctctgcac agggaaacctt tgcaccaag agagttatga	180
ctatctcaag actctggctg gtatgttca tattgtgaga ggagacttcg atgagaatct	240
gaattatcca gaacagaaaa ttgtgactgt tggacagttc aaaattggtc tgatccatgg	300
acatcaagtt attccatggg gagatatggc cagcttagcc ctgttgcaga ggcaatttga	360
tgtggacatt ctatctcgg gacacacaca caaatttga g	401

<210> 191
<211> 406
<212> DNA
<213> Homo sapien

<400> 191	
tggcagcccta agccgtggga gggttccagt cgagaatggg aagatgaaag acttcagatg	60
gaacagaaaat aaatgccttt tttgacaaac gcagcagtgc gtgcctctag cttgcaagag	120
cgttactccc cttcatagct taaaagggtt ttgcactgc gtgcagttt agtagctaaa	180
tcttgtgtga cgctccacaa acactgtaa gaattttgca gagaaagata accgttgcac	240
cccaatgccc cccacaggca ttctactccc cagttacctt taggtggga gaaatggta	300
agagttgttc ctacaacttg ctaaccttagt ggacagggtt gtatgttgc atcatccgga	360
tagatgtgaa gaggacggct gttggataa taattaagga taaaat	406

<210> 192
<211> 316
<212> DNA
<213> Homo sapien

<400> 192	
cccgccccggg ccctggcat aaaactttaa atttacttag tgttacttaa tgtatattct	60
aaaaagagaa tgcagtaact aatgcctaa atgtttgatc tctgtttgtc attacttttt	120
caaaattatt ttttctgtt aagtataata tataaaacctt cttgtttaaa ttgaatttct	180
atattatgtgg ttaattgcag tttattaaag ggatcattat cagtaatttc atagcaactg	240
ttcttagtgtt ttgtgtttt aaaacagaat taggaatttgc agatatctga ttatatttt	300
catatgaatc acagac	316

<210> 193
<211> 146
<212> DNA
<213> Homo sapien

<400> 193	
gaaacatgga ctgccccctt aattttgact gtcctaaaaa cctatttctg atttataata	60
tgctgcctga taaagtgcaca ctagatgtac cagctgagtg ttatcttc ccatcacaga	120
tcagatttgc gcatatccacag gtattt	146

<210> 194
 <211> 405
 <212> DNA
 <213> Homo sapien

<400> 194

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cgatgtgct cactgacatt ctactccaag tcggagatgc agatccactc caagtcacac      60
accgagacca agccccacaa gtcccacat tgctccaaga cttcgccaa cagtcctac      120
ctggcccgac acatccgtat acactcagg gctaagccct acagttgaa ttctgtgag      180
aaatcctcc gccagctctc ccacccatc cagcacaccc gaatccacac tggtgataga      240
ccatacaaat gtgcacaccc aggctgtgag aaagccttca cacaactctc caatctgcag      300
tcccacagac ggcaacacaa caaagataaa cccttcaagt gccacaactg tcatcggcgc      360
tacacggatg cagcctact agaggtgcac ctgtctacgc acaca      405
  
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<210> 195
 <211> 421
 <212> DNA
 <213> Homo sapien

<400> 195

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agaattcggc acgagctact cttgcgcgc tggcactccg cagccttaa gttcgcgcg      60
ggggccaggc aagagttac catgaagagc ctaagtccc gcctgaggag gcaggacgtg      120
cccgcccccg cgctgtctgg cgccgcgcgc gccagcgcgc atgcagcaga ttgaaataaa      180
tatgtgacc gattgtgaa agcagcagaa aggggggatg tagaaaaagt gacgtcaatc      240
cttgctaaaa agggggtcaa tccaggcaaa ctagatytgg aaggcagatc tgtctccat      300
gttgtgaccc caaaggggaa tcttgagtgt ttgaatgccca tccttataca tggagttgat      360
attacaacca gtgacactgc agggagaaat gctttcacc tggctgctaa gtatggacat      420
g      421
  
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<210> 196
 <211> 476
 <212> DNA
 <213> Homo sapien

<400> 196

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agaattgatc tatagattta atgcaatgcc tactaaaatc ccagtacgt ttttacagg      60
catagacaat agacatagcc aaaacttatt ctaaaataca tatgaagatg cacaggccct      120
agttatacaa tcttgacaaa gaagaataaa gtggaaagaa tctatttgat ttaaggctt      180
accatgtaac tacagtcatc aagagagtgt ggtatcggca gacggtcaga catacagatc      240
aatgaaatgt aacagaggac ccagaaatag gcccacacag atatgctaa tggatattg      300
acaagcgtgc aaaacaattc aatgaaagaa taagcttca aaaaaatggc gttggagcaa      360
ccggacatcc ataggaaaaa atgaacccat acctaaacca taaaccttat ataaaaataa      420
acacaaaatg aatcataggc ttaaatgtaa gctataaaac ttttagagaa aaacac      476
  
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<210> 197
 <211> 503
 <212> DNA
 <213> Homo sapien

<400> 197

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tagccctcg tgaagccccca gaccacagct atgagtcct tcgtgtgacg tctgcgcaga      60
aacatgttct gcatgtccag ctcaaccggc ccaacaagag gaatgccatg aacaaggct      120
tctggagaga gatggtagag tgcttcaaca agatttcag agacgctgac tgcggcgg      180
tggatctc tggcagga aaaatgttca ctgcaggtat tgacctgatg gacatggctt      240
  
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ctgccgtcca tgggggctgc attggcggag gtgtggacct tgtcacccgc tgtgacatcc	420
ggtactgtgc ccaggatgct ttcttccagg tgaaggaggt ggacgtgggt ttggctgccc	480
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<210> 198
 <211> 168
 <212> PRT
 <213> Homo sapien

<400> 198
 Phe Val Ala His Ser Leu Ser Ser Ala Ala Ala Arg Ser Arg Leu Cys
 1 5 10 15
 Pro Lys Glu Glu Thr Val Thr Asp Leu Glu Thr Ala Val Leu Tyr Pro
 20 25 30
 Ser His Ser Ser Phe Thr Met Pro Gly Ser Leu Pro Leu Asn Ala Glu
 35 40 45
 Ala Cys Trp Pro Lys Asp Val Gly Ile Val Ala Leu Glu Ile Tyr Phe
 50 55 60
 Pro Ser Gln Tyr Val Asp Gln Ala Glu Leu Glu Lys Tyr Asp Gly Val
 65 70 75 80
 Asp Ala Gly Lys Tyr Thr Ile Gly Leu Gly Gln Ala Lys Met Gly Phe
 85 90 95
 Cys Thr Asp Arg Glu Asp Ile Asn Ser Leu Cys Met Thr Val Val Gln
 100 105 110
 Asn Leu Met Glu Arg Asn Asn Leu Ser Tyr Asp Cys Ile Gly Arg Leu
 115 120 125
 Glu Val Gly Thr Glu Thr Ile Ile Asp Lys Ser Lys Ser Val Lys Thr
 130 135 140
 Asn Leu Met Gln Leu Phe Glu Glu Ser Gly Asn Thr Asp Ile Glu Gly
 145 150 155 160
 Ile Asp Thr Thr Asn Ala Cys Tyr
 165

<210> 199
 <211> 168
 <212> PRT
 <213> Homo sapien

<400> 199
 His Arg Gly Gly Glu Met Ala Phe Ser Gly Ser Gln Ala Pro Tyr
 1 5 10 15
 Leu Ser Pro Ala Val Pro Phe Ser Gly Thr Ile Gln Gly Leu Gln
 20 25 30
 Asp Gly Leu Gln Ile Thr Val Asn Gly Thr Val Leu Ser Ser Ser Gly
 35 40 45
 Thr Arg Phe Ala Val Asn Phe Gln Thr Gly Phe Ser Gly Asn Asp Ile
 50 55 60
 Ala Phe His Phe Asn Pro Arg Phe Glu Asp Gly Gly Tyr Val Val Cys
 65 70 75 80
 Asn Thr Arg Gln Asn Gly Ser Trp Gly Pro Glu Glu Arg Lys Thr His
 85 90 95
 Met Pro Phe Gln Lys Gly Met Pro Phe Asp Leu Cys Phe Leu Val Gln
 100 105 110

Ser Ser Asp Phe Lys Val Met Val Asn Gly Ile Leu Phe Val Gln Tyr
 115 120 125
 Phe His Arg Val Pro Phe His Arg Val Asp Thr Ile Ser Val Asn Gly
 130 135 140
 Ser Val Gln Leu Ser Tyr Ile Ser Phe Gln Pro Pro Gly Val Trp Pro
 145 150 155 160
 Ala Asn Pro Ala Pro Ile Thr Gln
 165

<210> 200
 <211> 132
 <212> PRT
 <213> Homo sapien

<400> 200
 Gly Gln Glu Lys Ser Leu Ala Ala Glu Gly Arg Ala Asp Thr Thr Thr
 1 5 10 15
 Gly Ser Ile Ala Gly Ala Pro Glu Asp Glu Arg Ser Gln Ser Thr Ala
 20 25 30
 Pro Gln Ala Pro Glu Cys Phe Asp Pro Ala Gly Pro Ala Gly Leu Val
 35 40 45
 Arg Pro Thr Ser Gly Leu Ser Gln Gly Pro Gly Lys Glu Thr Leu Glu
 50 55 60
 Ser Ala Leu Ile Ala Leu Asp Ser Glu Lys Pro Lys Lys Leu Arg Phe
 65 70 75 80
 His Pro Lys Gln Leu Tyr Phe Ser Ala Arg Gln Gly Glu Leu Gln Lys
 85 90 95
 Val Leu Leu Met Leu Val Asp Gly Ile Asp Pro Asn Phe Lys Met Glu
 100 105 110
 His Gln Ser Lys Arg Ser Pro Leu His Ala Ala Ala Glu Ala Gly His
 115 120 125
 Val Asp Ile Cys
 130

<210> 201
 <211> 120
 <212> PRT
 <213> Homo sapien

<400> 201
 Met Leu Val Leu Val Leu Gly Asp Leu His Ile Pro His Arg Cys Asn
 1 5 10 15
 Ser Leu Pro Ala Lys Phe Lys Lys Leu Leu Val Pro Gly Lys Ile Gln
 20 25 30
 His Ile Leu Cys Thr Gly Asn Leu Cys Thr Lys Glu Ser Tyr Asp Tyr
 35 40 45
 Leu Lys Thr Leu Ala Gly Asp Val His Ile Val Arg Gly Asp Phe Asp
 50 55 60
 Glu Asn Leu Asn Tyr Pro Glu Gln Lys Val Val Thr Val Gly Gln Phe
 65 70 75 80
 Lys Ile Gly Leu Ile His Gly His Gln Val Ile Pro Trp Gly Asp Met
 85 90 95
 Ala Ser Leu Ala Leu Leu Gln Arg Gln Phe Asp Val Asp Ile Leu Ile
 100 105 110
 Ser Gly His Thr His Lys Phe Glu

115 120

<210> 202
<211> 135
<212> PRT
<213> Homo sapien

<400> 202
Arg Met Cys Ser Leu Thr Phe Tyr Ser Lys Ser Glu Met Gln Ile His
1 5 10 15
Ser Lys Ser His Thr Glu Thr Lys Pro His Lys Cys Pro His Cys Ser
20 25 30
Lys Thr Phe Ala Asn Ser Ser Tyr Leu Ala Gln His Ile Arg Ile His
35 40 45
Ser Gly Ala Lys Pro Tyr Ser Cys Asn Phe Cys Glu Lys Ser Phe Arg
50 55 60
Gln Leu Ser His Leu Gln Gln His Thr Arg Ile His Thr Gly Asp Arg
65 70 75 80
Pro Tyr Lys Cys Ala His Pro Gly Cys Glu Lys Ala Phe Thr Gln Leu
85 90 95
Ser Asn Leu Gln Ser His Arg Arg Gln His Asn Lys Asp Lys Pro Phe
100 105 110
Lys Cys His Asn Cys His Arg Ala Tyr Thr Asp Ala Ala Ser Leu Glu
115 120 125
Val His Leu Ser Thr His Thr
130 135

<210> 203
<211> 135
<212> PRT
<213> Homo sapien

<400> 203
Leu Leu Leu Ala Arg Trp His Ser Ala Ala Phe Lys Val Arg Ala Gly
1 5 10 15
Ala Arg Gln Glu Leu Ala Met Lys Ser Leu Lys Ser Arg Leu Arg Arg
20 25 30
Gln Asp Val Pro Gly Pro Ala Ser Ser Gly Ala Ala Ala Ser Ala
35 40 45
His Ala Ala Asp Trp Asn Lys Tyr Asp Asp Arg Leu Met Lys Ala Ala
50 55 60
Glu Arg Gly Asp Val Glu Lys Val Thr Ser Ile Leu Ala Lys Lys Gly
65 70 75 80
Val Asn Pro Gly Lys Leu Asp Val Glu Gly Arg Ser Val Phe His Val
85 90 95
Val Thr Ser Lys Gly Asn Leu Glu Cys Leu Asn Ala Ile Leu Ile His
100 105 110
Gly Val Asp Ile Thr Thr Ser Asp Thr Ala Gly Arg Asn Ala Leu His
115 120 125
Leu Ala Ala Lys Tyr Gly His
130 135

<210> 204
<211> 167
<212> PRT

<213> Homo sapien

<400> 204

Ala	Leu	Gly	Glu	Ala	Pro	Asp	His	Ser	Tyr	Glu	Ser	Leu	Arg	Val	Thr
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Ser	Ala	Gln	Lys	His	Val	Leu	His	Val	Gln	Leu	Asn	Arg	Pro	Asn	Lys
				20				25				30			
Arg	Asn	Ala	Met	Asn	Lys	Val	Phe	Trp	Arg	Glu	Met	Val	Glu	Cys	Phe
					35			40			45				
Asn	Lys	Ile	Ser	Arg	Asp	Ala	Asp	Cys	Arg	Ala	Val	Val	Ile	Ser	Gly
				50				55			60				
Ala	Gly	Lys	Met	Phe	Thr	Ala	Gly	Ile	Asp	Leu	Met	Asp	Met	Ala	Ser
					65			70			75			80	
Asp	Ile	Leu	Gln	Pro	Lys	Gly	Asp	Asp	Val	Ala	Arg	Ile	Ser	Trp	Tyr
					85				90			95			
Leu	Arg	Asp	Ile	Ile	Thr	Arg	Tyr	Gln	Glu	Thr	Phe	Asn	Val	Ile	Glu
					100				105			110			
Arg	Cys	Pro	Lys	Pro	Val	Ile	Ala	Ala	Val	His	Gly	Gly	Cys	Ile	Gly
					115			120			125				
Gly	Gly	Val	Asp	Leu	Val	Thr	Ala	Cys	Asp	Ile	Arg	Tyr	Cys	Ala	Gln
					130			135			140				
Asp	Ala	Phe	Phe	Gln	Val	Lys	Glu	Val	Asp	Val	Gly	Ileu	Ala	Ala	His
					145			150			155			160	
Val	Gly	Thr	Leu	Gln	Arg	Leu									
					165										

<210> 205

<211> 381

<212> DNA

<213> Homo sapien

<400> 205

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gaggaaaaaa	agaaatctgc	attttaattc	atgtggtca	aagtcaatt	actatctatt	120
tatcttatat	cgttagatctg	ataaccctat	ctaaaagaaa	gtcacacgct	aatatgtattc	180
ttacatagtg	cttgtatctgt	tgcatttgcgt	ttaatttgcgt	gaaaagtatt	gtatctaact	240
tgttattactt	tggttagtttc	atctttatgt	attattgata	tttgtaattt	tctcaactat	300
aacaatgtag	ttacgctaca	acttgcctaa	aacattcaaa	cttgtttct	tttttctgtt	360
gttttctttt	ttaatttcatt	t				381

<210> 206

<211> 514

<212> DNA

<213> Homo sapien

<400> 206

aaaagtaaat	tgcataaaat	tacatccaat	ttctttctct	aaaccaacat	attcttcacc	60
ttcacaaagc	aaacacatgg	tgcactgaaa	ccgaggtgtt	accagttta	catactgttc	120
tgccatttgt	ggggggtgca	accacaacat	aagtcaagaa	aaaagctatc	cagttttcg	180
tggaatctgg	tgaagtttac	acttagcgat	aagcctctaa	gcctgaactt	agcagggcta	240
gcaaaaactt	atttatttcc	taactcctat	tattttagaa	tggtttcaa	aataatactg	300
caagttccca	atgaaataac	aaaacagaac	aaaaagctgt	gagaatctt	ttttttctt	360
tggctcccta	aagacttgga	ataatttata	ttagtgttgc	atacattta	ctttctacat	420
tttgatgtac	ttgcttctga	aagcactaga	acaaattaat	tgaaataaaa	cctctctgaa	480
accatttgaa	tctttgatcc	taccatagag	ttt			514

<210> 207
<211> 522
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(522)
<223> n = A,T,C or G

<400> 207
caagctttg gtcatagca gcccgtgg aaggcattctg agtgcgttgt ctgcctggt 60
gggtttcatt atccgtctg tcaaacaggc caccttaaat cctgcctcac tgcagtgtga 120
gttggacaaa aataatatac caacaagaag ttatgtttct tacttttatac atgattca 180
ttataccacg gactgtata cagccaaagc cagtcgtggct ggaactctct ctctgtatgt 240
gatttgact ctgctggaaat tctgccttagc tttgtgtact gctgtgtgc ggtggaaaca 300
ggcttactct gacttccctg ggagtgtact tttctgtctt cacagttaca ttggtaattc 360
tggcatgtcc tcaaaaaatga ctcatactg tggatatgaa gaactattga cttcttaaga 420
aaaaaggggag aaatattaat cagaaagttt attcttatgaa taatatgaa aagttaacca 480
ttatagaaaaa gcaaaagcttgg agtttctttaa atgttaagctt tt 522

<210> 208
<211> 278
<212> DNA
<213> Homo sapien

<400> 208
aaaatgcact accccctttt tccaaacacgg agcttaaaac aaatataatga aagagtggaa 60
aattcaaaaat aaggggcaaga gataaggttt ttttttttt tcctttaaga tagactcagg 120
ataggttagat agctttcact gatgttagatg tggatataat ttttttttca ggaaaaaaaaat 180
tccccaaacat cttatgaaaaa agtataacaac ttttttttca aatatgttat ttactcactg 240
ccaaagacag ttttatttga aatcttgggg ctgtattt 278

<210> 209
<211> 234
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(234)
<223> n = A,T,C or G

<400> 209
cctcccaaattt ttagcaggtt ctgggnagga ccctaggag tggtttatgg gggctagctg 60
gtgaaactgc ctttcctttt ctgttctatg agtgtgtatgg tggttgagaa aatgtggggc 120
tatgggttcag gcgcaactca catgtgcaaa gatggagaaaa gcactcacct acacgttttag 180
gctcagaatg ttgattgaaa cattttgaat gatcaaaaat aaaatgttat tttt 234

<210> 210
<211> 186
<212> DNA
<213> Homo sapien

```

<220>
<221> misc_feature
<222> (1)...(186)
<223> n = A,T,C or G

<400> 210
aaaataactg atggcaaaat aaaanattt catcacatca tactgtgtaa acatgttaagg
tctctgtaca aagaaaatata catgcaaaat aatgtaaaaa tttaactgaa ataataaaag
aaacaataca caaataaaaaa ttatgagggtt acgaatacac atccagttc gaatccaatt
tctttt                                         60
                                              120
                                              180
                                              186

<210> 211
<211> 403
<212> DNA
<213> Homo sapien

<400> 211
aaaaatttgtt aaaatatttt agtacaaaat aagtagcttc cagcgagggtt tttataccat
agtaagagca cacaatagat attactagca cacatgggtt atctggagc gctatacgta
caataaacct aattatggaa cagaaaatttg cattctgttt ccagtgcac tacactccta
ctttctcaaa agtctgctct attaatatca gctcagtgca gtttactatg aatagttat
gtctgtatg caaagcatta attgtctct ttttacaaac atacatttt ttcataagga
agactggggg aaaacccaga aacatacaga gaaaaggaaa gcatcatcaa atatatgtta
aaaattaaga ttagtgggtt tactagtcat cctacaacaa ttt                                         60
                                              120
                                              180
                                              240
                                              300
                                              360
                                              403

<210> 212
<211> 345
<212> DNA
<213> Homo sapien

<400> 212
cctctttatg agttcattttc tgctgttcag tctcggcaca cagacacccc tggcaccgg
ggtgtacttt ctactctgtat cgctgggcct gtgggtgaga taagtccacca gctacggaa
gtttctgacg tagaagagct taccctcca gggcatctt ctgatcttcc accatttca
agggttttaa taggaataat aataaagtct tcgaatgtgg tcaggtcatt tttggatgaa
ttaaaggcat gtgtggcttc taatgatatt gaaggcatg tggcctcac ggctgctgtg
catattatcc tggttattaa tgcaggtaaa cataaaagct caaaa                                         60
                                              120
                                              180
                                              240
                                              300
                                              345

<210> 213
<211> 318
<212> DNA
<213> Homo sapien

<400> 213
aaaatgtttt attattttga aaataatgtt gtaattcatg ccagggactg aaaaaagact
tgagacagga tggttattct tgtcagctaa ggtcacattg tgccttttgc acctttctt
cctggactat tgaaatcaag cttattggat taagtgtat ttcatacgat attgaaagg
caatagttaa agtaatgagc atgatgagag tttctgttaa tcatgttata aaactgtt
ttagcttac aaatatgtca gtttgcagtt atgcagaatc caaagtaaat gtcctgctg
ctatgttaagg attgtttt                                         60
                                              120
                                              180
                                              240
                                              300
                                              318

<210> 214
<211> 462
<212> DNA
<213> Homo sapien

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<400> 214
aaacacatct gttctggca gcaaggata ttatgcattt agagcaatag gtgcctgaa 60
agttattgtt gctttttt cagtttggtc gtgtcacttg aatcagaaac 120
caaacacatg taaaaaaaata tcatcccaa tgcccccat taactctctc tccagaaggt 180
gacaatgtta gtgaactcaa gacttcact gatgatggta ttttacaatg aaaacacaag 240
gaaaccctt gaggtccaat ttccatca tattctccaa atagaaaaat agcagctcta 300
catgttgatg aaaagaaatt tcaatttctt cctattgtt tttactcata tcaacattaa 360
tatgtatctg gatttattaa ttccaaaaaa gaaaatttta gttaccaaattt atttcagaaa 420
ttaataaaag cattatatat atgtaatttag cacttatcta cc 462

<210> 215
<211> 280
<212> DNA
<213> Homo sapien

<400> 215
aaactttct gaaacgatta gctgttagcca aattatgtgg ttacgtttg ctacattaga 60
atttggaaat gcaatatgtg tggttaatct actgtttgaa atttataatg gtctctgata 120
tgattcgaat ttggtaact ttggaaagtt attttcccccc tttagtcatg gatttctatt 180
tgtttttaa tgtaatttt tctagaaagc atctgaattt actaggctt tcctatataa 240
aaaactcaaa acttgtaac tctgtacttt aataaaattt 280

<210> 216
<211> 210
<212> DNA
<213> Homo sapien

<400> 216
aaaatctctg gttccaaagt ttctgggaa aaggtcgggt tacccacat ttttgttcc 60
cattagtaat attctaggtt cctcacaaaa ttttgcgtt tgccatggct gtttgtttt 120
agtgggtgct gtaggattaa ttccaaaaata ggcagaattt cattccccc aagggtggcaa 180
aaattagcta tactgatgtt attgtcattt 210

<210> 217
<211> 398
<212> DNA
<213> Homo sapien

<400> 217
ctggagctgc tagaacttga gatgagggca agagcgatta aagccataat gaaagctgg 60
gatataaaaa agccagccata ggtatttaac ttgatttga attttggta tgtttgaaca 120
aagccacatc attaattttt gtatctaaaa ttatgggtt gtcttatatg ttatctca 180
tgtaaccctt attaggactc atttttagccc taaattacct gtggctgtt ctttttattt 240
ttttgactac ttatattta taaatgtgtt ttactgtctt atgaattcat ggcaatata 300
ttggatagcc tggatacttt gtttagatgatg ttttagctg tgctgcataa tcttaaaagc 360
cattagcaaa gagtcgtggt attttttct ttatctt 398

<210> 218
<211> 487
<212> DNA
<213> Homo sapien

<400> 218
ctgcgcgg tcaggctgg taaagatcag gtccccagg accttgcgtt ttatgtcgcc 60

attctccagc aagacctcg	tgccgaagac ctctacgatg	cggcggtggg cagggtatcc	120
tggctgcacg acgtgccgg	ccatcacgtc cacgtcaatc	accgcacagc ccagttcag	180
tgttttaca cattatattt	ttataatctc acaataacta	taaatttaggt agaacaggaa	240
atgaggtttg gagaagatac	ttgacttatac cgaccatctg	tacttgtccc atagtaagga	300
gcctcaagca gagacaaagg	aggaagttgc ctatgttgc	tggttacag gccataaaatg	360
aatgtcatct tttcctccc	ctggggaaaa atgtctcaa	aatcccacca taggacatga	420
catctccaga acctctatta	caaaatacac attcctgt	gagggtaac aaatttgggt	480
taacctg			487

<210> 219

<211> 390

<212> DNA

<213> Homo sapien

<400> 219

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accatcaaca ttcttcaagt atctgaaata	ctattaatta gcaccttgc	attatgaaca	120
aaacaaaaca aggacctrac	ttcatctctg tctaggtcag	cacctaacaa tgtggatcac	180
actcatggga aagtgtttt	aggtagttt aacccttgg	agtttgggtt ttaaacttcc	240
ctctgtggaa gatattcaa	agccacaagt ggtcaaatg	tttatggttt ttattttca	300
atttttat	tggtttctt acaaagg	acatttcca taacaggtgt	360
aaaaaaaaagt tcaaattttt	gggggagcgg		390

<210> 220

<211> 341

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(341)

<223> n = A,T,C or G

<400> 220

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gtaaaactg tgaataac	tttctnnnca aaaggcaat	attgaagttt tttatcaact	120
tcgctagaaa aaaaaaaaaa	cttggcatac aaaatattt	agtgaaggag aagtctaacg	180
ctgaactnnn aatgaaggga	aattgtttat	gtgttatgaa catccaaagtc	240
tttaagtgt caaagaagct	tccacaaaat	tagaaaggac aacagtctg	300
tcgccttaaa ctctggacac	tctatatgt	agctgttaatt a	341

<210> 221

<211> 234

<212> DNA

<213> Homo sapien

<400> 221

ccagggggaa ttgagggagg	ctctaagcta ggggcactgc	atggtgggac aggatggccc	60
cttggggact gaaccctggg	gagaagacaa acagtaataa	taaaaaacaaa taacaagtac	120
tttggggatg gattgtatga	cctatagtga cagatgacat	cactaataact gaaagcttct	180
tatattaata atttggcaa	aatgtcattt	tgtaatatacg tatatgtttt ccag	234

<210> 222

<211> 186

<212> DNA

<213> Homo sapien	
<400> 222	60
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	180
	186
<210> 223	
<211> 486	
<212> DNA	
<213> Homo sapien	
<400> 223	60
ccataaggcag ataagtagca gttcaactgg atgtctctt tctccaaatg ctacagtaca aagccctaag catgagtggaaatcggtgc ttccagaaaag acttcaaata acacttaatt gtgcctggct gtgcgtggatgtatattctgtgtcatttttt cttcatggaa gaaacagccc acagagctca ccaacaagta ctccaaaact aagtaagagt ttaagctttt agatgcaaca agatgagcta atcgaaaagc ccatgtctcc tatgcgtac gcacgatctg gtctggaaac agcagagatg aatggcaaactcatagctgc aggtggctat aacagagagg aatgtcttcg aacagtcgaa tgctataatc cacatacaga tcactggtcc tttcttgctc ccatgagaac accaagagcc cgatttcaaaa tggctgtact catgggccag ctctatgtgg taggtggatc aatgg	120
	180
	240
	300
	360
	420
	480
	486
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<211> 322	
<212> DNA	
<213> Homo sapien	
<400> 224	60
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	180
	240
	300
	322
<210> 225	
<211> 489	
<212> DNA	
<213> Homo sapien	
<400> 225	60
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	180
	240
	300
	360
	420
	480
	489
<210> 226	
<211> 398	

<212> DNA
 <213> Homo sapien

<400> 226

caaggccccca ccgcagagca cacctatgct atggggagcc ctgctggcag ccccgagac	60
catgccatgg cctgcaggag ccaggctcct gtgtggatga agtcctctt cctctgtgcc	120
ttgatccctt ggggggtgcct ttggtcatct cttctgtcct ttcctgtctc tgaaatagtc	180
atcaactcccc ttgactctct ctgttcacgt cttctcagtc tgcaagtttta acttctgtaa	240
ggagtttaat ctgggggttcc aagaaaacaa gttccttgaa aacatagcac tgactttgca	300
acaatagaaa actaacaat gagcaacaat ataaagagta gagtagttc tcattgggtg	360
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<210> 227

<211> 535

<212> DNA

<213> Homo sapien

<400> 227

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tgggtccata agaaaaaaact gtatgtaaaaa tggttaggac aaacaataaa gtagaaacag	180
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tcacaaacca gtaaaagtata aagacaccat ggagaaatgg ttaactctgc cccaaacacc	300
caacagcaaa caaaaccaga atgaataagg ctttggcaga caattttaga aatttgaatg	360
ttacatttct caataattca caaacaatat attatatggt atatttatat taaatattgg	420
gaaaccaatg ttgtaaattt gatgcttata atgcttttagc caatgagagc acaatgatat	480
caatcaagct aaatgaatgc tgggttatac acaacagtgc tcatttatga aacaa	535

<210> 228

<211> 301

<212> DNA

<213> Homo sapien

<400> 228

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tgctttgtt tgtttggta aagcttattt ccattgtggt gcggctatgg	180
agactgtctg gaaggcttgg aatggttat tgcttatggt aaaatttgc tgatttctta	240
caggcagcgt ttggaaacct tttattatat agttgtttac atacttataa gtctatcatt	300
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<210> 229

<211> 420

<212> DNA

<213> Homo sapien

<400> 229

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attacctatg ggttatatac ctcaaatacg acattctgtt caaatgtttt gtaatataac	180
caatgttttca aatgttattc tgctcataaa agagcagatt tttatttgaac ttgtgcaata	240
actatattac catacaataat aatatttcat gaatgtttc ccaagtcgg agcgaccaca	300
tagggagaaaa atgcaaatgt ctcaattttt gttcacaaaa gtatatttta tcaaatttgc	360
gtaaagctgtg gatagcttaa aagaaaaaaa gttcctgaa atctggaaa caagacattt	420

<210> 230		
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<212> DNA		
<213> Homo sapien		
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<210> 231		
<211> 389		
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<213> Homo sapien		
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<212> DNA	
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tggctacaca ctctcactac acacacAGAC cccacAGTC tATATGCCAC aaacacATT	180
ccataacttg AAAATGAGTA ttttgcataAT ctcagttcAG gATATGTTT ttacaAGTTA	240
atcctaaagt cataaAGCAA gaagctattc atAGTACAAG attttatttG ctaagcttt	300
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tacAGCTCCT ATTGATAGGA catAGTggAA GTGAGCTACa ACgtAGTACG tGTCGTGTA	180
· tacAGATGTC AGTgATGAGT ttGCTAATAC AATGCCCAGTC AGGCACACtA CGGTGAAAAG	240
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GGTGAATAT GCTCGTGTG CTACGTCAT TCTACTGTA AATATATGGT GTGCTCACAC	420
GATAAACCTT AGGAAGCCAA TTGATATCAT AGCTCAGACC ATACCTATGT ATCCAAATGG	480
tt	482
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<212> DNA	
<213> Homo sapien	
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ccgAGAGGAC AGAATGGATA TAATCTGAAT CCTGTTAAAT tttctctAAA ctgtttctta	300
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<210> 238
<211> 374
<212> DNA
<213> Homo sapien

<400> 238
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acactcatgg atatgtaaaa actgtcaaga taaaattta atagttcat ttatttgta      180
ttttatgtt aagaaatagt gatgaacaaa gatcctttt catactgata cctgggtgt      240
tattattga tgcaacagtt ttctgaaaatg atatttcaaa ttgcataag aaattaaaat      300
catctatctg agtagtcaaa atacaagtaa aggagagcaa ataaacaaca tttggaaaaa      360
aaaaaaaaaa aaaa      374

<210> 239
<211> 200
<212> DNA
<213> Homo sapien

<400> 239
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ccgggtggca agaagctctg tgtgactttt tttgtgggtt tggggagtt gtaaggtgat      180
ggctgtgggg actgtgggtt      200

<210> 240
<211> 314
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(314)
<223> n = A,T,C or G

<400> 240
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atattaaaaa ggaaactaat tggaccattt tctatttgc tattttatac aaaaaggcta      180
cacaattgat acactctatt cagataacaa tcaatttagag tgantatgaa ttactggcga      240
caccatcaact caattcttaa aaatttagaaa ttgctgtagc agtattcaact ataacttaac      300
actaccgaga gact      314

<210> 241
<211> 375
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(375)
<223> n = A,T,C or G

<400> 241

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ggctgcctac agtgctgctt cattgttagt gggtaagaa ttcaagacca aaaagccct	180
tctgatttat ccaatctttt tattatacat ttatctttt tcgttatata ctgggtgtg	240
atccaaggta tacatgaata gaaaaagatg gtgttaaatt ttttgttagg ctgggaattc	300
tngctaaagg aatggnaaaa aacctgnnt tgnaaaattn acntgtccca aagnnaagga	360
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<210> 242	
<211> 387	
<212> DNA	
<213> Homo sapien	
<400> 242	
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ttaggccccac ctatgttaatg ctgttataact agctaattgtg cccatttggaa tagttcaagg	180
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ctgttactgt agccgagttt cccttcgtct ccacacatat gtagtggat cttgcaggat	300
ttccatagttt ccaatttatca aaggccttga ctacttagca ttgctgtattt acagatgtgc	360
aaactgaggc actgaaaaagt caaatttt	387
<210> 243	
<211> 536	
<212> DNA	
<213> Homo sapien	
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<221> misc_feature	
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acactctgac acatgctctg agaataactgg gactgctgtt tcaaaaaaaaaa aggttcaaac	180
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ttcacatcaa gagtacccca agaaaaacga aatccatggc acanacactg tacaagggtg	360
cagggcaggg ctctgagggg cccaaacccc atttgccaa ctcgattttc tagcattgaa	420
gggagcaagg ggtcaggcat atgatggaga tgatactgaa atgatttatac caaaatccat	480
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catctggact tttagaatctg gcacacaaca aaagtgcctg gcatccacta ctgctgcctt	240
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tgctttgcta accaaagagc atatatttta ctgtcag	397
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<213> Homo sapien	
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gaacgaagtt ggaaaaatca agcccatatc ttgccgaaat gtaaatggct attcctacaa	240
agtggcagtc gcattgtctc ttttcttgg atggttggg gcagatcgat ttaccttgg	300
ataccctgct ttgggtttgt taaagtttg cactgttaggg ttttgtggaa ttgggagcct	360
aattgatttc attcttattt caatgcagat tgggacct tcagatggaa gtatgttacat	420
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aacgcaatta tatccataaa tattttt	508
<210> 246	
<211> 358	
<212> DNA	
<213> Homo sapien	
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gatttgcgaaat tagtagttt tgaatgtaaa taaaattcca gttataatag	120
tggctacaca ctctcaactac acacacagac cccacagtcc tatatgccac aaacacattt	180
ccataacttg aaaatgagta tttgcataat ctcagttcg gatatgttt ttacaagtta	240
atcctaaagt cataaagcaa gaagctattc atagtacaag attttatttgc taaagcttta	300
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<211> 673	
<212> DNA	
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aagaatataa acctcagggt gaccgaaaaa tcagaatagg tgggtata gaatgggtc	600
tcctnctccg cggggcnaa gaaggtggtg ttgangttc cggncgttta ntgtatagn	660
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<210> 248
 <211> 149
 <212> DNA
 <213> Homo sapien

<400> 248
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<210> 249
 <211> 458
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (458)
 <223> n = A,T,C or G

<400> 249
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 ggcacaggag gatctctaaa gcagtagcca aacaccactt tgtaaaagga ctcttccatc 180
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<210> 250
 <211> 374
 <212> DNA
 <213> Homo sapien

<400> 250
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 <212> DNA
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<211> 387	
<212> DNA	
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<210> 255	
<211> 225	
<212> DNA	
<213> Homo sapien	

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<220>
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<223> n = A,T,C or G

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<210> 256
<211> 544
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (544)
<223> n = A,T,C or G

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ccttgcttaa agcccagaag tggtttaggc ntggaaaaa tctggttcac atcataaaga      60
acttgatttg aaatgttttca tataaaaaaca agtgctaagt gtaccgtatt atacttgatg      120
ttggtcattt ctcagtccta tttctcagtt ctattattti agaacccagt cagttcttta      180
agattataac tggccctaca taaaataat gcttctcgat gtcagattt acctgtttgc      240
tgctgagaac atctgtgcct aatttaccaa agccagacct tcagttcaac atgcttcctt      300
agctttcat agttgtctga catttccatg aaaacaaagg aaccaacttt gtttaaccca      360
aactttgttt gtttacagtt ttcagggag cgtttcttcc atgacacaca gcaacatccc      420
aaagaaataa acaagtgtga caaaaaaaa aacaaaccta aatgctactg ttccaaagag      480
caacttgatg gttttttta atactgagtg caaaaaggnc cccaaattcc tatgtgaaa      540
tttt      544

<210> 257
<211> 420
<212> DNA
<213> Homo sapien

<400> 257
aaatgtcttg tttcccagat ttccaggaaac ttttttctt ttaagctatc cacagcttac      60
agcaatttga taaaatatac ttttgtaaac aaaaattgag acatttacat tttctcccta      120
tgtggtcgtt ccagacttgg gaaactattc atgaatattt atattgtatg gtaatatagt      180
tattgcacaa gttcaataaa aatctgtctt ttgtatgaca gaatacattt gaaaacattt      240
gttatattac caagacttgg actagaatgt cgtatggag gatataaacc cataggtaat      300
aaacccacag gtactacaaa caaagtctga agtcagcctt gtttggctt cctagtgtca      360
attaaacttc taaaagtttta atctgagatt cttataaaa acttccagca aagcaacttt      420

<210> 258
<211> 736
<212> DNA
<213> Homo sapien

<400> 258
aaacaaaatg ctaaacctaa aaacattgtt ctgtcagttc ccaaattaaa tctacttaga      60

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acaaaaacaa aaatttatag ctcggtcaca tactacttaa ataatattgt tcaggcatct	120
ctaaaatcct ccatgtttc aagtatggaa atagaactca aatattccac aatacagtac	180
taaacagatg gagtatttag gaaagacttt gttgtcatat ggcacaatat taatatttg	240
ttgcttcaat acgtttgaa ataaatatca gatTTTGTt ttttttccct aaaagaccaa	300
aattataatc tacattaaga taattctgac tgtggtaag acttaagagt gtAAAATACA	360
acatcaatat ttatcacaa aagtAAAGCT ggtaacaaat tataaaagga GCCAGTACTC	420
tactgagaca ggctcgaga ttaaagctca tcatgataga aatAGTCATC atggagctgt	480
ctgccataat ctgtggcttc actggtgaga aacaAGTCCG ggTTTCCAG aatCTCTCT	540
tcagagagct ttTGTcacc attCAAATCC atttcatcaa ttagatgaag CGCCTCCTCT	600
tgtgcaatgc cctgattatt aggtCTACCC aaggtAACAG CTCTGGGA TCAAGCCTGC	660
catcgTtATC ttgtcataa tcattcaccg aatCTGTCTT tctcacaagt atcccattct	720
ggatCTTCAT ttgcag	736

<210> 259

<211> 437

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(437)

<223> n = A,T,C or G

<400> 259

aaaaccatac taaaatcatt taccaaataa cnaagatctt aatctaaaag atagtgaata	60
catcatcatc atgaaaatctg gtttatgtg ctctatgaag tactggaga attgctttt	120
tatTTTCTT ttgctttatt aggtcacaca aaacagaatg aattAGCAGA AAAATGTATG	180
ttataaaaca gcatTTTACTA CTTCAATTa ATTtTTTTA CTAACAATTG TGGACCTTT	240
tGATGACACT TATGTATGTt TTAAATAAT TATGTACTTA TTAGTACTTA ATGAGCCCTT	300
CCTGCCTCAA TATAAAATTa CTAAACTTGG AGAATTACAG ATTtATTGT AGGCCCTGAT	360
GTTAGTCACT TTGGAGAACG TAAAAATTG GAAATGATGT AATTCCCACT GTAATAGCAT	420
AGGGATTTG GAAGCAG	437

<210> 260

<211> 592

<212> DNA

<213> Homo sapien

<400> 260

tttttttttT gaaaaatata aaatttaat aaaggctaca tctcttaatt acaataatta	60
ttgtaccaag taatttcct taaatgaact ctttataatg cataatttac agtataagta	120
gaacaaaatg tcatgacaaa agtcattgag tacaAGACTT gtaataaaaaa ggcataaaaat	180
atatttatac ataaacccct ttcaaaaaac aaggGAAAGC ttgagccctc aatataGGGc	240
gacacacgga gcgggtgacc gtgcaggtaC aggtactgtt ctgattttaa gtcaAGCACT	300
agagatagtG gattaataCT CTTTGCCTG acactatata cagatgtata gtacaAGTAA	360
caatggcaaA cagaatgtac agattaactt aacacaaaaa cccgaacatc AAAATGAAGG	420
TGTGTTGAGG AAAGGTGCTG CTGGGTCTCC ctacaactgt tcatttcttT GTGGGGCAGG	480
GGGTAGTTCC TGAATGGCTG TGGTCCAATG ACTAATGTAa AACAAAACA GAAACAAAAA	540
AAACAAAGGAA CTGTCATTc cacgaaAGCA CAGCGGCAgT gattctAGCA GG	592

<210> 261

<211> 450

<212> DNA

<213> Homo sapien

<400> 261	
gtggcagggc ccagccccga accagacaag ggaccctca aggagctca ttcttagcatg	60
agaaaaattga gaagtaaaccc agaaagtac agaatgtctg aaggggacag tgtggagaa	120
tccgtccatg gaaaaccttc ggtgggtac agattttca caagacttgg acagatttat	180
cagtcctggc tagacaagtc cacaccctac acggctgtgc gatgggtcgat gacactggc	240
ctgagcttg tctacatgt tcgagttac ctgctgcagg gttggtacat tgtgacctat	300
gccttggga tctaccatct aaatctttc atagctttc tttctcccaa agtggatcct	360
tccttaatgg aagactcaga tgacggctc tcgctaccca ccaaacagaa cgaggaattc	420
cccccttca ttcgaaggct cccagagttt	450
<210> 262	
<211> 239	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1) ... (239)	
<223> n = A,T,C or G	
<400> 262	
taactttgat gacaaaatct aaaatcaaag anttagtctt aaaagcctat agtgacttgt	60
ttacttgcatttataattt ttcacttagt acaggctatt aatataagta atgagaattt	120
aagtattaac tcaaaaaaaag atagaggctc caaacttttc taagaaatta atgcattttc	180
aaagtaataa tataatcaat ctgttaagtca aaagtaattt catattcatt gccaaattt	239
<210> 263	
<211> 376	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1) ... (376)	
<223> n = A,T,C or G	
<400> 263	
aaaaaaaaaaaa aaaaaaaaaatt ctttgtngett tnttagagga aaaaaagaaaa aaccccaact	60
tttancactg atactacata ttgctctgtt aaagaatttt ctctgccaaa aaaaagaaaa	120
aacaaaaaaaaa cgcttaaagc tggagtttga cattctgctt tcagatgtcg tcttttatt	180
agttagttagt gatggtttgc taataatcaa tagtaataa tttttgtaa tcccatcaag	240
tggctccata tggctctgtt ctctcggtac tggtaatgt tttactgtt gtaccttaaa	300
gccgaaatca gtaactatgc atactgtaac caaggtattt ggcttacaga gttgtttgtt	360
gnataaaagaa aatttt	376
<210> 264	
<211> 207	
<212> DNA	
<213> Homo sapien	
<400> 264	
aaatttagcat tccacaaaata tacaggtaat ttaataatata ttgtgcattga atacatacac	60
aatgcttata tataaaaaattt ccagtttgtt ttcatgtgtt ggcaagggat ttgtataacaa	120
tcataagctg tggcatattt ggtccattt aatattcaca atacaaaagc acaaaaagaaac	180
cattgatttta caaaaggaaa tctattt	207

<210> 265
 <211> 388
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(388)
 <223> n = A,T,C or G

<400> 265

naactgcact ttatgttta ctgtaacatt nttttttaac t	tgatcaacca taagcatgca	60
aagnccnct gaaactgctt ccactgcctg ttgtatagaa a	tggtaaat tataaagggt	120
attcaatttgc gagtccttc ctttttata gcacttctaa g	ctgtgtgcg cyacacacac	180
cacagaggtt ggaaggacca cctttaataa attatcttct	taatcgcaga gaatttctga	240
agataaaaact gacaaaatgc taaacccaagg ctttgatgag	tcccaaagga ccacagatcc	300
atcggttcctt atttgaagaa ttcatcccct gtatgttct	agccttgta gggcaactgga	360
ttacaagatc caccaggct ctgaacaa		388

<210> 266
 <211> 616
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(616)
 <223> n = A,T,C or G

<400> 266

aaatacagag tcaaaaagatg atttataaaa tntaaaacat t	tttctgcttg gccgtatttg	60
aagacaagct gaatacatat ctatgttctg aataagtcca c	tatggatat atataggaag	120
agatatacat atatccatcc acagatacac acacacatat a	tatctgc atgtatatat	180
acataattct ttctatagtt acagggaaata cttcttctat a	attctgatt ttgactccca	240
tcctccacca tttaactcatc cactcattac ctaaatcttg	gtttcttcc tatattgta	300
aataatccat ccaaacttct agccagtact gtcaggaggg	ttcttgctcg agtgagctgt	360
taatactatt ttccactgac aacttctgca catcgaggac a	acagtgtatc tgaagactcc	420
gctgtatact tccaacaacg gggcatttt tcttcgttag tc	ggcatgac aattacttta	480
taggaagact cttcacgaat atcaccacct tctaagttga tg	gagaattt cccttaagc	540
tcgattacat ctgcagtcat ctctcggtt tcctgaccag taa	agtttgac tcagaaggca	600
tcatattaattc attcaa		616

<210> 267
 <211> 341
 <212> DNA
 <213> Homo sapien

<400> 267

ccattatgtt tttttttt taaaaataac ttatccagc tacttatttt	taatagttac	60
ttattcttgtt tttttttt ttgtatgtca ttgtatgtttt g	tatataattt ttgatattaa ccccttgta	120
catgtataat ttgaaatat ttctccctt ttttagttt tcacattctg	ttcattgtat	180
cagattctgtt gcagcagttt ttaatttga agtgtatctga ctgacttgg	tttgcatttttgc	240
tgtcctggat tatttagttt aaatcaaaaa acttgctgcc cagaccaatg	ttatgggct	300
ttcactctat ttttggtag tagtagtttta agagttttag g		341

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<210> 268
<211> 367
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(367)
<223> n = A,T,C or G

<400> 268
ttgttagattg gaatagcaaa agtgaatgct ntgacccaaa ttttgcct cctaaataaa      60
gacgtntcct tctagagagc aaatctatca taaaatgtca aaactagaag agaataaaaat    120
gaaaggaaaa aacctagaaa aatatctaa aatatcaaataat gcagtcattt ctaaatataa    180
gccataatta tagcttacc tattgttctt attgttccta tgctgcttct acaatgttac    240
atcaactata cttagcttta ctctccaaa atcttggtga tgaaggcttc tgagtgtgct    300
ttccaatgtg ccagaaccag aagggcattc caaggcttcc ccacatttcc tccatttacg    360
gagacag                                367

<210> 269
<211> 270
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(270)
<223> n = A,T,C or G

<400> 269
caaatctctc cctcaactaga cgtaagccnt ttnctcaactc tctcaatctt atgcatacata  60
gnaangcngn tgaggtggat taaacccaaac ccagctacgc aaaatcttag catactcctc    120
sattaccac ataggatgaa taatagcagt tctaccgtac aaccctaaca taaccattct    180
taatttaact atttatatta tcctaactac taccgcattcc ctactactca acttaaactc    240
cagaccacg accctactac tatntcgac                                270

<210> 270
<211> 368
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(368)
<223> n = A,T,C or G

<400> 270
ctgaatcatg aataaacacta tataatagag tntaaggaac acaagcatta gatgtgatcc  60
ttgccccata cccttagatt atgtcagact aaagctgaca attctgccag gctctgaacc  120
cctagtgccc ccaacccaaa tcttggaaagc aaagaatatg ccctgtcata caactttgta  180
caagttgttag taaaacaaag cttaagtttt ctcatcttcc tacagcaaataat ggtcagttat 240
ttaataaaaca ctaaaatgct cctaagaatc cattttgagt ttgttacca aacacattgt  300
gcaagaactg actacacaaa aagttccctt gaaatttggc ccacaaattc acttaagggtt  360
ggaaattt                                368

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<210> 271
<211> 313
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(313)
<223> n = A,T,C or G

<400> 271
aaatttatat aaaactctgt acatgttac tttattattg cataaacagc ataatcttca      60
agacaanngt ttgcaaacac atgtccaatt caggaaaaaa aatttcacgt ttctcgcttg      120
gtttttct tccttttat ttgttggga gattcccagc tagttcaga ctggctgt      180
gaaggaggca cactattttgc ttgggtattt gacttggatt tatctgtctc ttgttagtatt      240
ggcggcactt gggaaagagct ttgtcagaa tcacttttgc ataagattac agatggctcg      300
gtagaagtag cag      313

<210> 272
<211> 462
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(462)
<223> n = A,T,C or G

<400> 272
aaaaaacatt tatttaata agactattgc naacacatta aaaaaactaa atagtaatat      60
tacaaaatct atatacttgc acatttagta tttgtcaatg tgccagaggt ttcttcatg      120
aaatttgact tcttgaagt gaaggcttt ttctatcatc tcttatacgct ctgactgaat      180
aagtcttaat gcttcttca tgtttctat caatagggtt aaatcccag gctcatatgt      240
gtacaatctg ttagagtatc ttccagctat gtcagctcta actgttaaag aagggtctac      300
aaacatgatt cttaggcacat attgccatc aggtgataaa ttcttcatc tggttcatg      360
cataaggttt agcatgatga acttattctg agccatttct tgtatttctt cattttggc      420
aaatacttca ttttagtgctt gagagtattt acaatcctcc ag      462

<210> 273
<211> 282
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(282)
<223> n = A,T,C or G

<400> 273
ctgatcaaag catggatat tttaatagtn ttatacataa tattttaca tagaaaactt      60
tacatnnat ttcatattat ataattctgc ttattcttc aaaaatttac acatccattg      120
ggcaaggaat ggtttctt aaattacaa tattaaatgc acttaatcat tgtgtatagg      180
ttaaaccaaa gtaactatta actaactttt aggcattta aggaggtaaa acatacattt      240
tacacataag tatttgatgc aaatatgcag ataaaatttt tt      282

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<210> 274
<211> 125
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(125)
<223> n = A,T,C or G

<400> 274
cagccctaga cctcaactac ctaaccaacn ttnctaaaaa taaaatcccc actatgcaca      60
ttnaatcnct ccaacatact cgattctac cctagcatca cacaccgcac aatcccstat      120
ctagg                                         125

<210> 275
<211> 528
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(528)
<223> n = A,T,C or G

<400> 275
aaagctgtgg aaaagcttta ttatagattt ttntacagaa ttaaaaaagt tcaaacaata      60
ataagccngg aaccacaaat aattaaaagg aaacacagca atcccataaa caagcattct      120
ggcatctgtt agaaaattttc cctcaaatta tgaaatgtag ctctccatgc tttccaatga      180
ttgttataat acccacaat atctgtgatt tcagtgaaat actttaacaa aagttttctt      240
ttaaggcat gatcctgatt catttttct tcaatatctc agtcattca ggaactacct      300
taaataaaatc tgcaactatt ccataatctg ccacttgaa aattggagct tctgggtctt      360
tattaattgc cacaattgtc ttgctgtctt tcatacccagc taaatgttgg atggctccag      420
atattccaac agcaatataa agttctggtg ctactatTT tcccgctgn ccaacttgca      480
tgtcattggg aacaaagcca gcatcaacag cagcacggga agcaccaa      528

<210> 276
<211> 420
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(420)
<223> n = A,T,C or G

<400> 276
aatgtcttg tttccagat ttccaggaaan tttttttctt ttaagctatc cacagctac      60
agaaacctga taaaatatac ttttgtaac aaaaatttag acatttacat tttctcccta      120
tgtggtcgct ccagacttgg gaaactattc atgaatattt atattgtatg gtaatatagt      180
tattgcacaa gttcaataaa aatctgctct ttgttatgaca gaatacattt gaaaacattg      240
gttatattac caagactttg actagaatgt cgtatttgag gatataaacc cataggtaat      300
aaacccacag gtactacaaa caaagtctga agtcagccctt ggtttggctt cctagtgtca      360
attaaacttc taaaagttt atctgagatt ctttataaaaa acttccagca aagcaacttt      420

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<210> 277
<211> 668
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(668)
<223> n = A,T,C or G

<400> 277
ccaggggtggc tctgatatacg cagccctggc ntatttcgat tatttcagga agactggcag      60
atngcaccagg accctgaatt cttagtgc tcctcaatccc attttatccc atggaaaccac      120
taaaaaacaag gtctgctctg ctccctgaagc cctatatgc ggagatggac aactcaatga      180
aaatttaaag gaaaaaccct caggcctgag gtgtgtgcca ctcagagact tcacctaact      240
agagacaggc aaactgcaaa ccatggtgag aaatttgacga cttcacacta tggacagctt      300
ttcccaagat gtcaaaaacaa gactctcat catgataagg ctcttacccc cttttaatt      360
gtccttgctt atgcctgcct cttagtgc ttgcaggatgtat gctgtcatta gtatttcaca      420
agaagtagct tcagagggtta acttaacaga gtatcagatc tatcttgtca atcccaacgt      480
tttacataaa ataagagatc cttagtgca cccagtgact gacatttagca gcatctttaa      540
cacagccgtg tggcaaatg tacagggcgc cttagtgcagat ttggacttct agactcacct      600
gttctcaactc cctgtttaa ttcaacccag ccatgcaatg ccaaataata gaaattgctc      660
cctaccag                                         668

<210> 278
<211> 202
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(202)
<223> n = A,T,C or G

<400> 278
aaatttggat cgacggcaac caggggaagn tnctaaactc ctaatctatt ctggatccaa      60
ttngcnaagt ggggtccccat caaggttcag tggcagtgga tctgggacag atttactct      120
cacgatcagc agtctgcaac ccgaagattt tgcaacttac tactgtcaac agagttacat      180
gtccccgtac acttttggac cc                                         202

<210> 279
<211> 694
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(694)
<223> n = A,T,C or G

<400> 279
ctgtacttgg acaaaataag ttaattctat ttgggtgtcc attaaagttt tatgtggcta      60
tgnaccact ggagctaaaa attggctttt aactgtttcc aaatcagaac tagcagagga      120
gagaagtaaa taaagccat ggcactccct tcagaggctc aaaatggta gattttgatg      180

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cagatttaac	cttagcgagt	ttcagtcagt	ccatTTAGAT	gatCCTGTA	gttCATACAA	240
atacactgaa	ccgtTGGTT	aactTCCTT	cCTTCCTCAA	agTTTATGAT	aaAGAGACTC	300
atCCCTGTAT	TGGAGTGAC	TGACATAAGT	TCAAGATCTGC	TCAAGATGGC	TGGTAAGGAA	360
cacttaaggt	cAGTCAGAAA	ataatcaaAC	agactTC	TGTAAGCACC	GTGACTCACA	420
actaagacac	TGGCTGCTAA	TCCTGGAATA	CCGCTGTCTG	AATTAACCTT	AGAGCTGTGA	480
ttttTCCTA	AAGGAAATAT	CTCTGCCAAA	GAAGTTCCA	GACAGNTGCT	TGGGAGATCC	540
ttggggaaaaa	CTGGTCTTT	TGATCCGTT	CTTCANGAN	TAGGTNGACA	AAAGAAATNC	600
aaaaaaagnct	ATCCCACGCN	TTTNTCACCT	GGGCCAGCG	GNNTCCCTCC	RGGGGGGGGGN	660
aaacacangg	gactCTTCCC	NGGGCTNGCT	TNNG			694

<210> 280

<211> 441

<212> DNA

<213> Homo sapien

<400> 280

aaaaaaacttc	CATGCAACTT	CTGGTTATT	GTTGGCAAC	TCCACATGAT	AAAAAAATAA	60
aaacagccca	ACCGAGTTTC	GGAAATTAAAGT	ACTCTCTAG	TAAGTGATT	AAACTTGTA	120
tatTTGCCAC	AGGACTGACT	TATTTATTA	CTAGCTAGAA	GCTCTTAAGT	TCACTTGTT	180
atcaggGCAT	ATACAGAAGG	GTTGTTAAA	ACTCGATGTT	AACTTACAA	CTTTCTGACC	240
tggTGCATGA	ATTCTCAAGT	ACTGTATTC	ACTGTGTTGG	TGTGTCTGAT	GGAAATTTCG	300
aygtggTCCC	ACAAAAATAT	TTTATGTTAGT	GTGCCTTCAA	AGAGAACCAT	TTATTCTCT	360
TCACTTATCG	TCCACAAAG	TCACATTGG	TGGTGGTCAG	CCAAGTCGCA	TCTGGTCTAG	420
TTTACTCTT	GTCCCAATT	T				441

<210> 281

<211> 398

<212> DNA

<213> Homo sapien

<400> 281

aaatTTGTTA	GGTCTGAAGA	ATCTAAAACT	GTTAATTAA	CCCTTAACCT	GTGCCTAGAA	60
actacAGCAC	ATATAAAATA	TGTAAACACC	AGCCTGTTGC	TGACTTTTC	TGCTTATT	120
acAGCCTCAA	ATATTCCTCA	TTATCTGTC	ACTTAGTTCT	TCACTTTCT	CCTTCTGACT	180
TTAATAATG	GTAATAGGAA	AACAAAACCC	AAAGCTTTTC	AGAACCTTCAG	TGTGAGGTT	240
CCTATTGTA	CAAGTTAACT	TGTAAATACT	CAGGTTTAC	GATGTATAAT	TTACCTAATA	300
GACCAAACTA	ACTCATGGAG	ATATTTGAA	CTATTATTA	GGTACAAACT	TTATAAAGAA	360
TGTTAGTATG	TCACTAAAATA	TAACATTACA	GCTTATT			398

<210> 282

<211> 226

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (226)

<223> n = A,T,C or G

<400> 282

aaaacaatat	TCTCTTTG	AAAATAGTAT	NAACAGGCCA	TGCAATAAT	GTACAGTGT	60
ttacnccaat	ATGAAAGAT	TCTTCAGGT	AACAAGGGT	TGGGTTTGA	AATAAACATC	120
TGGATCTTAT	AGACCCTCA	TACAATGGTT	TTAGCAAGTT	CATAGTAAGA	CAAACAAAGTC	180
CTATCTTTT	TTTGGCTGG	GGTGGGGCG	CCCAGGCCGA	GGCTGG		226

<210> 283
<211> 358
<212> DNA
<213> Homo sapien

<400> 283
aaacaaaaat actcaagatc atttatattt tttggagag aaaactgtcc taatttagaa 60
ttccctcaa atctgaggga cttaaagaa atgctaacag attttctgg aggaaattta 120
gacaaaacaa tgtcatttag tagaatattt cagtattaa gtggaatttc agtatactgt 180
actatcctt ataagtcatc aaaataatgt ttcatcaaattt gttaaatgg accactggt 240
tcttagagaa atgttttag gcttaattca ttcaattgtc aagtacactt agtcttaata 300
cactcagggtt tgaacagatt attctgaata taaaattta atccattctt aatatttt 358

<210> 284
<211> 288
<212> DNA
<213> Homo sapien

<400> 284
aaaacttttg ttaagaaaaaa ctgccagttt gtgcatttga aatgtctgtt ttgacatcat 60
agtctagtaa aattttgaca gtgcataatgt actgttacta aaagctttaat atgaaatttt 120
taatgtgaag ttttcattt ataattcaag gaaggatttc ctgaaaacat ttcaaggat 180
ttatgtctac atatttgtgt gtgtgtgt gtatatatat gtaatatgca tacacagatg 240
catatgtta tatataatga aatttatgtt gctggattt tgcatttt 288

<210> 285
<211> 629
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (629)
<223> n = A,T,C or G

<400> 285
cctaaaagca gccaccaatt aacaaagcgt ncannctcaa caccactac ctaaaaaatc 60
ccaaacatataactgaactc ctcacaccca attggaccaa tctatcaccc tatanaagaa 120
ctaatgttag tataagtaac atgaaaacat tctcctctgc ataagcctgc gtcagatcaa 180
aacactgaac tgacaattaa cagccaaata tctacaatca accaacaagt cattattacc 240
ctcactgtca acccaacaca ggcatgctca taaggaaagg taaaaaaag taaaaggaac 300
tcggcaaattc ttaccccggc tgtttaccaa aaacatcacc tctagcatca ccagtattag 360
aggcacccgccc tgccccagtgacacatgttta acggccgcgg taccccttaacc gtgcaaagg 420
agcataatca cttgnccctt aatttagggac ctgtatgaat ggcttcacga gggttcagct 480
gtctcttact ttaaccagt gaaatttgacc tgcccgtgaa gaggcnggca tgacacagca 540
agacgagaag accctatgga gcttaattt attaatgca acagnaccta acaaacccca 600
caggtcctaa acttacccaa accctggca 629

<210> 286
<211> 485
<212> DNA
<213> Homo sapien

<400> 286
aatgtactt gctcagctca actgcatttc agttgttta tagtccagtt cttatcaaca 60

ttaaaaccta tagcaatcat ttcaaatacttctgcaaat tgtataagaa taaagttaga	120
attaacaatt ttatTTgtA caacagtggA attttctgtc atggataatg tgcttgagtc	180
cctataatct atagacatgt gatagcaaaa gaaacaaaca aaaggccagga aaacactcat	240
tttcgccttg aatatgtaaa tgggattaaat ttgtcctgt gccttatgtg gaaagggact	300
tctttggttt tccttttttgc ttctggggaa agcatgtgca ggagacatat catccaaaca	360
taaaccattaa aatgtttgt ggttgcttg gctgttaattt tcaaagttagt taattgagga	420
caaagggtaa tgcagaagtg atagcttgg ttgtcgagt ctgttttaa gtggcctgat	480
tattt	485
<210> 287	
<211> 340	
<212> DNA	
<213> Homo sapien	
<400> 287	
cctggagtcc aataaccacc ccctcatacc acaccctgtg catacaccag ccaagcctt	60
cctggctcgg gaagggaaga gaaaaaagac gcaggccacc tgggggttct gcagtcttg	120
gtcagtccag ccttctatct tagctgcctt tggctccgc agtgtaaacc ttgcctgcc	180
ggaggcagga ggcccagctg gaccccgag ggccatgagc aggccgcgc catcttgcc	240
tcaagcttgc cttcccttg agtccctctc tcccctcgcc tctagccaga ggtgtagcct	300
gcagatctag gaagagaaga gctggggagg agatgaagg	340
<210> 288	
<211> 290	
<212> DNA	
<213> Homo sapien	
<400> 288	
aaacagtc tccctcggtgt tctccttgc aaactgttca tcccagtttc ctctgaaata	60
gacagcattc accagaacca gccttgc tggatccact gagcccgag agagcaactc	120
cgcaatttttta ctttctgtct tttcagctac ccaggtgttt atgttttc tggacttctc	180
tacggcgctg ataaaagtcaa gtcctccat ctctgcttgg tagaattttt ggcaggaatc	240
tctaaaagat gagaggaat cacaagactt ttccccaaag agcctgttgg	290
<210> 289	
<211> 404	
<212> DNA	
<213> Homo sapien	
<400> 289	
ccacccacgc ttaggttccc atcacactga tgactccggg tttggcgagc acaggagcgc	60
aaaccttttc acattcttc tgtgatccaa atttgttttc gtttccacca caacctccat	120
accagaatct tgcacagctt ttgggttttgc gatcatagta ccattttat ataaaatccc	180
tgcaagttcc ttctgttttc ggcaacttgc atatatctgt ttcaagtgaga gccaatggtt	240
ctgtgctcac cattagattt gatggttgaac tagaagctga ctttgcgttgc tggaggttgc	300
ggggctgaga ttctttgttgc tggaaacttc cgtggtaggt ggctctgacc tggagacccatca	360
ggtagcagac cacagccaca tggtatgtct gcccagcggc cagg	404
<210> 290	
<211> 384	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	

<222> (1) ... (384)
 <223> n = A,T,C or G

<400> 290
 ccaggcgctc cttgtcgca tcagggaggg tggcattgaa ctgctcatgg gctgtggtca 60
 gtccctggat ctccctcaatg gtgtgcacaa tgaagggtgtc ctgcaggtcc tccatggccc 120
 cctccatcca gttgttgaag ggtgcagccc gcttggcata ctccaagtac agctggtcaa 180
 tggtctccag cagtttctcg gtccgcctca gagcttcct tcgctctga gtttagggccc 240
 ccagattgtc ccactggtca cagatcttt gcaaacgggc gttgacactg ggtgagtc 300
 aatantccag ctcattgagc tcctgtgcga tggcggcaat ctgctccaca cggtccttgt 360
 gggcagccag gccactctcg aagg 384

<210> 291
 <211> 278
 <212> DNA
 <213> Homo sapien

<400> 291
 aaagtttatt ttacttattt ctttatcaact ttattgtatc atcaccattt gtttcataat 60
 gtaaaatacta tatgttgaac aaattaaatg tcaaaaatttt ttattaccat agtccatgtt 120
 aatagtgggg ctttcagggtg ttttagagatt tttttgttg ttgttaacat tcattgcaaa 180
 agtactagat ggtgtataac tctagagttt aatttttaagg gattccctaa tatgtataact 240
 atcttttat ctgaagtaat aaataaacaat tgatcttg 278

<210> 292
 <211> 177
 <212> DNA
 <213> Homo sapien

<400> 292
 ccttggcccg gtcattcttg tccagttga taggttcagg aaattcggtt tacagctcca 60
 cctccgttcc ctgttaagt gcattccgtg caatcgcttg .gaacgcctgc tccacgttga 120
 tggcctccctt ggcactggc tcaaagttagg gaatgttgg tttgctgttag caccagg 177

<210> 293
 <211> 403
 <212> DNA
 <213> Homo sapien

<400> 293
 aaaaagaagg acttaggggtg tcgtttcac atatgacaat gttgcattt tgatgcagg 60
 tcaagtacca aaacgttcaa ttgatgatgc agtttcata tatcgagatg ttcgctcg 120
 cagtaactgtt ggttaaatga caatttatgt ggatttgca tgtataacac agtgagacac 180
 agtaattttt tctaaattac agtgcagttt agttaatcta ttaatactga ctcagtgtct 240
 gcctttaaat ataaatgata tggtaaaaac ttaaggaagc aaatgctaca tatatgcaat 300
 ataaaatagt aatgtgatgc tgatgctgtt aaccaaagggg cagaataaat aagcaaaatg 360
 cccaaaagggg tcttaattga aatgaaaatt taattttgtt ttt 403

<210> 294
 <211> 305
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature

```

<222> (1) ... (305)
<223> n = A,T,C or G

<400> 294
aaagcaatct ggcatttgt cctgttagtga agcagaggat cataacataa gtaaactctc      60
tatgggtgga agtggagag aaggacattt tggcttgta catgaaaaga ctctccagat      120
agaaaacagat tctgcccata agtgaardaa aatgctttgt gggggtaatg agtgaattat      180
agtattcagg cagatgttac ataactgcta attaagtttc cctggattga nttanncaa      240
anaattgaaa gtngattttg gtcangtgtc agnnaaactac tgcctataaa cccatatcnt      300
accca      305

<210> 295
<211> 397
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (397)
<223> n = A,T,C or G

<400> 295
cctatcttgt tggcctttt gaagacacca acctgtgtgc tatccatgcc aaacgtgtaa      60
caattatgcc aaaagacatc cagctagcac gccgcatacg tggagaacgt gcttaagaat      120
ccactatgtat gggaaacatt tcattccaa aaaaaaaaaa aaaaaaaaaat t!ctcttctt      180
cctgttattt gtagttctga acgtagata ttttttttcc atggggtcaa aaggtaccta      240
agtatatgtat tgccgagtgg aaaaataggg gacagaaatc aggtattggc agttttcctt      300
tttncattt gggngaatt tttaatataa atgcggagac gtaaagcatt aatgcnagtt      360
aaaatgtttc agtgaacaag tttcagcggt tcaactt      397

<210> 296
<211> 447
<212> DNA
<213> Homo sapien

<400> 296
ccatcctcga tggtaagtt gtcgtggggc ccgaagacgt tggtgggat gacagcggtg      60
aagggtgcagc cgtactgctg gaagtagggcc ctgttctgca cgtcgatcat cctctggca      120
tacgagtacc caaaattgtt gttgtggggc ggcccattgt ggatcatgtt ctcatctatc      180
ggtaggtcg tcttgtcagg gaagatacag gtggacaggc aggacaccac cttgcggggc      240
cccacctcga agggcagtg caggacgttgc tcgttcatgt gcacgtttt cctccagaag      300
tccaaattgt atttgatatt ccggaacagg cccccccacca ttgcagcaag atggatgacg      360
tgtgtgagtt ggaccttctc aaacaggcg cgggtctgtc ctgtatccgt gagatcggcg      420
tcttagagg agacaaacac ccagtcc      447

<210> 297
<211> 681
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (681)
<223> n = A,T,C or G

```

<400> 297
aaataacagc atgtaaaata ttaaaataca agctttcaaa aataaaataca taaataagta 60
gaaccctcgta aagaaatagt caaacacatt aagtccttcc cagctgtccc tagaaagctg 120
ctgttctctt tttcattttc agctctggta agggcaggga ccaccctgca ggaagtgtca 180
atgatacgct gataagctt ttacttctct cctgtcagtt ggtgcctccc ctgtgtatgag 240
aaaagggtta ctgttgcagg tgctaaggaa ggctgtctt ctgtcactct gaagttgctt 300
ggagggtatgt ccccatgcag actctctccc agccctccac tcagggaaagg tctgtctgta 360
cccaactgcct tctatagcag aaaacttgca ctcctgaatg cttttttttt tttcaagaa 420
agaagnggct gnggactcaa cttagattctt ggtttggaaa agccaaaaca tattggtcac 480
tgattgtcac attgggttag aaatgtccat tcatgatctc ccttaagctg cacacaaccc 540
tatgaataaa ctaccattat ctaccctatt ttgctaaagc tcaaagagat taaaataatgt 600
tgacaggat cttagcctt aactcaactga aggngttact gcaaagttct gctcttcacc 660
aagaaggntt acaggccaaa g 681

<210> 298
<211> 353
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (353)
<223> n = A,T,C or G

<400> 298
cctggcttaa gaccagacat ttgaagaagg ctccaggcag ggaaaggaaa ggagaggcca 60
gccccacnct gncccccctccc tgccccacg tctccagcaa cacaaggcgg ccagtggacc 120
gtgaaccatt tatttccaaa ctataaaagaa acctgcttc tgagaaaana cactgcccag 180
gngatgaage tccagccct ggaggtccaa aaccctagtc aaactcagtc ccttttagaaa 240
gctgctgtgc ctggaaatg annntcggt gtcanagctt gggaaagtggt gggagaacc 300
agcccaactcc cctctcctgc tgcgattcca gcgcncgttg gncnccagatc tgg 353

<210> 299
<211> 560
<212> DNA
<213> Homo sapien

<400> 299
aaagttcaag gactaacctt atttattttgg gaaaggggag gaggaaggaa atgatatgg 60
acccagacac tgggcttaggc tgcaacttta tctcattta tactcccagc tgcgtatgtga 120
gaaagaaaagc aggctaggca tgtgaaatca ctttcatgga ttattaatgg atttaaagg 180
gcatcaatca gctcaactca agatttcata atcattttta gtatttagat tgcctctcaa 240
agttgttagta ctcacaata ctcactgg tttcctgttg taaaaacctt cagttagttt 300
gaccattgtg ctcttggctc ttgggctgga gtaccgtggt gagggagtaa acactagaag 360
tcttttagtac aaaactgctc tagggacacc tgggtattcc tacacaagtg atgtttat 420
ttctcataaa gagtcttccc tatcccaagg tcttcatgtat gccagtagcc atatatgata 480
aattatgttc agtgataact tagttatcag aaatcagctc agtggcttc cccgccatga 540
ttcacatttg atgagtttt 560

<210> 300
<211> 165
<212> DNA
<213> Homo sapien

<220>

```

<221> misc_feature
<222> (1)...(165)
<223> n = A,T,C or G

<400> 300
aaaaactaca taggggtgtg tgtgtgtgtg tatgtttatt ttatacacac atatttgat      60
attctaataat attactaagg caatttaat gaattaccat gtatataaaa aaatatctgn     120
cacttggcac acaggttgt atgtatgtt atatatataat gtatg                         165

<210> 301
<211> 438
<212> DNA
<213> Homo sapien

<400> 301
aaaatatatg tattaaaaaa caaaaagcaa cagtaatcta tgtgtttctg taacaaattg      60
ggatctgtct tggcattaaa ccacatcatg gaccaaatgt gccatactaa tgatgagcat    120
ttagcacaat ttgagactga aattttagtac actatgttct aggtcagtct aacagttgc    180
ctgctgtatt tatagttaacc atttccctt ggactgttca agcaaaaaag gtaactaact    240
gcttcatctc ctttgcgct tatttggaaa ttttagttat agtgttaac tggcatggat     300
taatagagtt ggagtttat ttttaagaaa aattcacaag ctaacttcca ctaatccatt    360
atcccttatt ttattgaaat gtataattaa cttaactgaa gaaaagggttcc ttcttggag    420
tatgttgtca taacattt                           438

<210> 302
<211> 172
<212> DNA
<213> Homo sapien

<400> 302
ccaaaacagg agtcctgggt gatatcatca tgagacccag ctgtgtctt ggatggttt      60
accacaagtc caattgctat ggtaacttca ggaagcttag gaactggctt gatgccgagc    120
tcgagtgtca gtcttacgga aacggagccc acctggcattc tattctgagtt tt           172

<210> 303
<211> 552
<212> DNA
<213> Homo sapien

<400> 303
ccagcctgtt gcaggctgct tcgttagcggt cgtcggctgc ggacttccct tcccgggtct    60
ggatcttttc atcctaccag atgagaaaagg gaatgagtga atggagttagtac cccgcacccct 120
gtcactttcc tgagacatga ctgccaggaa gaagagctgc tctggcttcc atcagggctg    180
gcaggacaaa ctgaccaggatg agtcagtagg cagagttcac actgaaaaag ggcacaagggg 240
ctgtcccaca atgggaggaa atggggcttc agaacttcta cttctctgaa aactaagaca    300
caattgggac aaccaccacc cccgtgttagtattctcacc tcgagacagg acaagatgaa    360
gttcacggct tcttctgggg taaagacctt gaagagccca tcacaggcca acaaaaatgaa 420
cctacaacac cagggagaaa tataaacggg ttttaggccc aaccaaaaaaa taaaaaataaa 480
aaaaagggcc tggagatgga gataaaataa atatttgtcc aactattcaa aggctaaggt    540
ttttttttctt tt                                         552

<210> 304
<211> 601
<212> DNA
<213> Homo sapien

```

<400> 304

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cctttgattc ttggtagtac attgcataaaatgtt aagaagctac ttttccttca      60
tgggaagaaa ttcccacatg agattcataaa attcttagac tccgtggctt ctttggtcg      120
aatgccttaa actcatatga gtgttctgga tcccagtgtt tccaatcata attcacat      180
tcacccatcac gaaccacata ctttgcccac ggtgaaatac gatacaagat ctctccgctt      240
ttacttagtaa taactacctt taatttggat ccatgaggca cgagtacaga tttattctgc      300
tttggggaa tatacagctc ccatttcca taatccagtt ttttgtatgg gtacgaaaat      360
ggattccaaac cattaaaatc tccagtaaga aaaactcctt ctgctcccg ggcccattct      420
ttgcagtata aaccaccatc agcacatctg tgacgccaa atgattcata gcctctggaa      480
aacttatcaa taccacccctt attttctcca atgttcttca aaatttggct aaactgctt      540
tacctgcgct ggaagtccac ggcgttagggc ttcaagtacc ggtcgatctc caggagtctg      600
g                                              601
```

<210> 305

<211> 401

<212> DNA

<213> Homo sapien

<400> 305

```
aaataaacagc atgaaaataa taaaataaca agctttcaaa aataaataaca taaaataagta      60
gaaccctcgtaa aagaaatagt caaacacatt aagtccttcc cagctgtccc tagaaagctg      120
ctgttctctt tttcattttc agctctggta agggcaggga ccaccctgca gyaagtytca      180
atgatacgtc gataagcttc ttacttctct cctgtcagtt ggtgctcccc ctgtgatgag      240
aaaagggtta ctgttcagg tgctaaggaa ggctgctctt ctgtcaactct gaagttgctt      300
ggagggatgt ccccatgcag actctctccc agccctccac tcaggaaagg tctgtctgtt      360
cccaactgcct tctatagcag aaaacttgca ctccctgaatg c                                              401
```

<210> 306

<211> 313

<212> DNA

<213> Homo sapien

<400> 306

```
aaactgacta tgattccctt gaaggcttgg cagttgttga tgatggcgat catgtactga      60
acgttagcgt gagggtgctg ccgattccctc aggtgctctt ctttatacag ctgcgccttca      120
tctttatatac tgaggacaga caggcttgg tcagacagca ctaagggcaa catggagctg      180
tttcaaatac cacgctgacg tcacgcctgg cctgaaattt cacatcacta acatctgacc      240
ggatgagcct ctaaaaataaa aacaatcttt agacgatcca gactaatggaa aggacagaga      300
ggttgattac ttt                                              313
```

<210> 307

<211> 366

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(366)

<223> n = A,T,C or G

<400> 307

```
aaagatgctg ntaatgaaca ttacggacaa ttcatggtgt ggctagttgg taacacttca      60
gctgattttt ctatgagat ggaaaaaaaaa aatcagccaa gtaagggcac atcttactt      120
catttataag tcagcatcca agttaaaaga attctctgtt ggacttgaca tcactcccat      180
```

cctctgatac tcgcctactc tcttctcaaa gaagtttagnt ctttccttcc antgaaat	240
tctcataaaa gtcaaattggg ttctctactc tgaaaacctt gctaaaaccc aattccagca	300
taagttgtc tgncacaaaac ncaatgnatt gcttcattaa antgcaattc atcccaatga	360
gcttcc	366
<210> 308	
<211> 534	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...{534}	
<223> n = A,T,C or G	
<400> 308	
ccagctatca gctgatcgac ttctgtctgg acgctcgatcc tgcttctgac atcaaaatct	60
tctgtctcaa agtcagagtc atccaaactcc tcaggggtcc ttatcatcg cactgcttc	120
ctgatgtccc ggatgccatc atataccagg cgaaaaagcat cgataaaactc attctcatcc	180
atgggcttggg cagggtccga gctgagggtt ccacccgtcg cttctacttg cttagtaaaa	240
cgtggcatga ctgtgttggg gagcagcttta gtggcttcca gaacccatc tgtgttagact	300
cctggctcat agtcgtccat ctctgagggtg actacgtgaa tgaccgggc tgcccgcc	360
cgaattgcac cagctgtgcg gccaggccat ccacatcctt ctcttggaga gcaatgacac	420
atttggtcac atcttccaaa atgtgattct ctgagacacgc caagaagtca tcaatggaa	480
taatgnacatc gacagcatct gtgagaacac cgacttggttt ttccatttgtt cttt	534
<210> 309	
<211> 164	
<212> DNA	
<213> Homo sapien	
<400> 309	
catactccctt acactattcc tcatacacca actaaaaata ttaaacacaa actaccaccc	60
acccccccta ccaaagccca taaaaataaa aaattataac aaacccttag aaccaaaatg	120
aacgaaaatc tgttcgcttc attcattgcc cccacaatcc tagg	164
<210> 310	
<211> 131	
<212> DNA	
<213> Homo sapien	
<400> 310	
aaaaatcatt tatcttcgg tgcttcaaca tgatgccaaa caaaaatcta ctgaataaaa	60
atagcaagga agggaatcaa acatttataa gatatattta ttattttct gaccaaaatg	120
caatgatttt t	131
<210> 311	
<211> 626	
<212> DNA	
<213> Homo sapien	
<400> 311	
cctatgtgcg ccagtttcag gtcatcgaca accagaacct cctcttcgag ctctcctaca	60
agctggaggc aaacagtcag tgagagtgga ggctccagtc agacccgcca gatccttggg	120
cacctggcac tcaagcactt tgcacgatgt ctcaaccaac atctgacatc tttcccggtt	180

agcaacttcc tgctccacgg gaaagaggc gatggattta cccctggacc cataagtctg	240
ttcatccatgc tgaagtcccc tccccattgc tccttcaagc caaaaactaca ctttgcttgt	300
tcctgtcccc tctgagaaaag gggatagaaa gtccttcct ctatgtcetc ccatcgagat	360
ctgttctggg gatggagctt ccaacttcct cttgcagcag gaaagaatgc tgctcacct	420
tctgtcttgc agagtggat tggggaggg attggcagcc ttcttctcca ccacctgtcc	480
agttcctcc tggtcagggc tgggacccccc aggaatatta tggccgtg tgggtgtgt	540
tgtgtgtgtg tcttctttta gggagcagga gtgcacatgg taattgaggg tagatgttg	600
gtgtgctggg gaggggtcct tctgtt	626

<210> 312
<211> 616
<212> DNA
<213> Homo sapien

<400> 312	
aaaccaaaga aattaagaaa aaagacttca ttgcttgaat gacgcgaaca gctgtctgag	60
tcaccttagac tttAACACCA cctggggccc tggaatgac gctgacgaga gatctgcaca	120
tagtaggcgt gggctccaaa tgtgcatac agctgactc acatcctac aagtcaagcct	180
cagatatgac ccaaggata cgtaccatct cttcttgaaa cagcgtgtca aattatatat	240
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tggtttaat gtgacctgtc atccccatct ttcgaattta tgagctccat cttctctaga	360
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cttaagcaca gtctctggca cagaataaat acgaaatgaa tgagtgaatg aatggatgga	480
tgggtgaaga gaaaaggcaa tgcacaagat ttacctatca aaatccacca atggcccta	540
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attaagaatt ctatgt	616

<210> 313
<211> 553
<212> DNA
<213> Homo sapien

<400> 313	
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gaaggactgt tttgttacaa actcaagcca gctacatgta tgctgcctt ggtatccctg	180
ctagagcaca tgcgggtata ataccgtatt atacacaaca aggccaccct gttgtatctg	240
tgttacaatt aaacatcaat cccagaaagt gaaccctagt catttattat aggtgccac	300
ctctgacttg gaacaaaatg ccactccatt catgttcatt tttgtcctgg agaggattta	360
tttcctaaaa gattctgaaa gccaaacaaat caatgttagt ttccatagag aacttaagag	420
taaggctcaa aatggccctca aaatggcattt ctggatgac ttccaaacagt gactggcctt	480
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aattggattttttt	553

<210> 314
<211> 330
<212> DNA
<213> Homo sapien

<400> 314	
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tgaaggttcc cagctgttct gccaggcaca ggaggacctc atcttcatca tagatggat	120
ctgttaaggaa aggcagaagc tcacttcggg tccttcaac cccaaaggccc aaggcgatgg	180
tggacagctt cttgatgctg ttgaggcgaa gctgaacgctc ctcatggcg agttcgctca	240
tgagcaccgc gatgggtac agcgagtcgt cgccgtcgcc cgccgcccattt tggctccgt	300

ccctttcctg tcagactgcg gccagcgctg	330
<210> 315	
<211> 380	
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<400> 315	
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ttaatcaagt catgaaattt gctttttaa agttcatttt aatgattatt cttccctct	180
aaagaaatga ttttgtaat gttgagaggt accttaccac aaatcctaactgta	240
ttcatggta ttttcaaag aattatgact cttccccaaa agaatcctaa aaaacttgt	300
ataaacctat aaagctgatt tgcatattta caaaattttt aatagcaa ataggcaact	360
catatatgtata tataattttt	380
<210> 316	
<211> 222	
<212> DNA	
<213> Homo sapien	
<400> 316	
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taatgtttta taaaagatag tggaaaaaa aaggtaatgc taaaataaag ggcgttttag	120
aaatatttaa ggacaacata aggtattaat atggaaaaaa aactgtacat atttcaagc	180
acaacactga aatattgcag cagtgtttaa ctgaattgtt tt	222
<210> 317	
<211> 490	
<212> DNA	
<213> Homo sapien	
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aaactgccta tcctgggtac tcttcttaag agaaaactgaa gagttgttc agcagtttt	180
acaagaattt gggacctccg cttgcttctt ttttccaaat atttggacac tttaggttgt	240
ttttgtttt tctttcaga tggtaatgtg aaagaaaggg tggcattttt acatatttcc	300
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tcccactgtg tggatgtgtg tatatgtatg tttgaatat gtttcttta taaaaaaaata	420
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gcaacatgtt	490
<210> 318	
<211> 340	
<212> DNA	
<213> Homo sapien	
<400> 318	
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gtcagtccag ctttctatct tagctgcctt tggctccgc agtgtaaacc ttgcctgcc	180
ggaggcagga ggcccgctg gaccccgag ggccatgagc aggccagcgc catcttggcc	240
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gcagatctag gaagagaaga gctggggagg aggtatgtt	340

<210> 319		
<211> 373		
<212> DNA		
<213> Homo sapien		
<400> 319		
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gctgatttt cttatgagat ggaaaaaaaa atcagccaa ag taaggcaca tcttcagttc	120	
atttagaagt cagcatccaa ggtaaaagaa ttctctgttg gacttgacat cactcccattc	180	
ctctgatact cgccctactct ctctcaaag aagtttagtct ttccctccag tgaaatattc	240	
tccataaaatc caaatgggtt ctctactctg aaaacccgtc taaaaccccg ttccagcata	300	
agtctgtctg ccacaaaactc aatgttattgc ttcatcttgc tgcaattcat gccaatgagc	360	
ttcacaggca agg	373	
<210> 320		
<211> 509		
<212> DNA		
<213> Homo sapien		
<400> 320		
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tttgcttcct taagtttca acatatcatt tatatttaaa ggcagacact gagtcgtat	180	
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acatgcaaaa tccacataaa ttgtcattt accaacagta ctgcacgagc yaacatctcg	300	
atatatgaaa actgtcatcat caattcaacg ttttggtaact tgaaactgca tcataaatgc	360	
aacattgtca tatgtgaaaa cgacacccta agtcttctt tttaaaaatg acattgcgtt	420	
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<210> 321		
<211> 617		
<212> DNA		
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<400> 321		
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tcctccctcc cacttgccag ggaacttttt tttgatgggc tccttttattt ttttctactc	300	
ttttcaggcg cacttgcgtt aaatggtaa ttcaaaaaaa aggtgactat ggtataatt	360	
gagccctctg gtccaggctc cagtttacct aatattacct cagaaaggat atggaggaa	420	
gatgtatctt ttgccaggctc tgactttct tcctgctccg ccctccatta acgctcagta	480	
ccctttagca gctgacggcc ccacgttcta ctccatgttt ggcttcctt ccaactagct	540	
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<210> 322		
<211> 403		
<212> DNA		
<213> Homo sapien		
<400> 322		

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tcaagtacca aaacgttcaa ttgatgatgc agtttcata tatcgagatg ttcgctcg	120
cagtactgtt ggttaaatga caatttatgt ggatttgca tgtaatacac agtgagacac	180
agtaattta tctaaattac agtgcagtt agttaatcta ttaatactga ctcagtgtt	240
gcctttaaat ataaatgata tggaaaac ttaaggaagc aatgctaca tatatgcaat	300
ataaaatagt aatgtgatgc tggatgtt aaccaggc cagaataaat aagcaaaatg	360
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<210> 323	
<211> 298	
<212> DNA	
<213> Homo sapien	
<400> 323	
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cacattgaaa ttggggctt cattctagat gtatgttgc cagatgtgc aggaaaatag	120
aaaaacctac catctcagtg agcaccagct gcctccaaa ggagggcag ccgtgttat	180
attttatgg ttacaatggc acaaaattat tatcaaccta actaaaacat tcctttctc	240
tttttcctg aattatcatg gagtttcta attctctt ttggatgtt gat	298
<210> 324	
<211> 78	
<212> DNA	
<213> Homo sapien	
<400> 324	
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ataaaccatt gtgtacat	78
<210> 325	
<211> 174	
<212> DNA	
<213> Homo sapien	
<400> 325	
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tgtatcatatc ctgcagctct gtttgcgtt ggttctgtcc caggatctc atcactgtcc	120
ccaaactccat ggttgtata gtgcgcatctc catcctgttc aaagagggag aagg	174
<210> 326	
<211> 679	
<212> DNA	
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<222> (1)...(679)	
<223> n = A,T,C or G	
<400> 326	
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aacttactct taaaaaggat ggntgccaag atggaaatgc ttactgggtt ttcatgtttaa	120
cctattcttt ggacataact atgaatttg tatacatgc acttcatgaa aagttgtgc	180
tccccagat tgcccacaag tgtatcttgc aagtcctaaa cattgtcca tgtaagcttc	240
aaaacagcgt taactgagtt attcaagtag cagttactaa agatacaatt cttgaagcag	300

tttcaatgg ttcgtatcca aataatcagt ttctgaacat tactacttca cataatagag	360
tccatcttca gtttcttctc actttcttcc tccttttg gtttcctttt tgtggctgta	420
ggccaccagt tccttggta ctatcaagat acttccatca tgggtacact ggagagcata	480
gtggttggta ttgactggcc taccttggtc atctcttaat ctactaaaa tatcatgata	540
aaggtcatgc agtttctgtt tcattatgtt aatagctttg gtacattgtg cttgctct	600
cttaanagtt tccttcttgc cttgcaagtt acatacatca tcttctaaat tcaaaaattat	660
gtccatttttgc gcgtttacc	679
<210> 327	
<211> 619	
<212> DNA	
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<223> n = A,T,C or G	
<400> 327	
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cagttaccaa agcctanata cgcgttagat ggcgcctttc cggtctgtgc gtctgctctg	180
gttcctctca ggcagcaaag ctgggaagg aagtcaggc aggagctcc ccgacgcccc	240
aacggcacaa gcagcagcta aagcaccgca ctttgctcta ctaacctttt acttaaatga	300
ggttttgcca aatccacatc tggaaccgcg tcacacccat ttgcaaggat gtttgttctt	360
tgtatgaaact gcatctctac tgcacatgag gccttcatt gtaggacaag aggagagttc	420
gtttatTTTT gtaactgttt tacatgttcc gattagttaa tcggtagctt atgtcatttg	480
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cttgggtata atttatttag ccgggatttg tgtgtcatgt tagagcaact ctaattcaag	600
aatagtgaca acttttaag	619
<210> 328	
<211> 132	
<212> DNA	
<213> Homo sapien	
<400> 328	
aaatccaaat acaaaggcat agtctctgca agatTTGTT ctttgaattt cttgatattg	60
taattgatta ttgataactg tcatcatgaa attatctctc aataataaga taaataaact	120
agcatatgaa tc	132
<210> 329	
<211> 854	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(854)	
<223> n = A,T,C or G	
<400> 329	
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catcaaggat acaaattctac agtagccaa tggcggttc atagtgtata atttattatc	120
aataaaaatttactccgttac aatcagcatt catttcctcc aataaaatt aagcataaac	180

cctaggtagt aacttctgc acatatgtat agctccgaat ttccctca	240
gcaaaaacaa tattcaagct tgtctgatta tgcatat	300
tataacaatag acaagacagg actatataga taatggacag acttaaatgc ccgcattt	360
aaggtaggaga aaatgatgaa tctatgcac cccgagaaca cttaaaat	420
cactggaaa ttcttacagc tacttacaa tcata	480
acatattcca ctacagagct atactctatg caactgttt ttcccctcat	540
agttcaaatt gaattctatc ttccacaatc acaatgggtg catcacccag tacacagaag	600
tttgaatcac aaaacataat taccacaata aaacacagt	660
aatctgccgc acaaactgca aattaaatta actacacaga cttaaaaacta tacagctac	720
catcacagtt gtgcattata aaaaagggag ttcttc	780
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<210> 330

<211> 299

<212> DNA

<213> Homo sapien

<400> 330

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tccatg gattctcaa atttatggtt aaagaggcac ttatacactc	180
tgcctcacc agcttgtgtat ttccacaaa aacgctcccg atcatctcg	240
ataaaatgcgt gctaagtga aagtcatccg atgacagctc agccacccgg agaatggctt	299
tcttgca	
ttccagaaact tgaatcttgg gttcttttc ttctgc	
ttcaccagg	

<210> 331

<211> 573

<212> DNA

<213> Homo sapien

<400> 331

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agcaaaatgt tcaagttaaa aaaaaacat accgggttag caatgcacta aaattatcca	120
catgaaaaca aatggtctgt aatcttataa accaacatag catttactg tcaacaatgt	180
gaaaattaa tatcttctca aacaggcata agatgaagaa gtgctat	240
aaggaactt tgaatgtaa aattacatta taattttca ttccgaattt acaaattgatt	300
tcaaaaacaa ggatcaaagt ttgactgca atagtaatgc aatataattt cataaaaatc	360
cttcaatttca tatttttca ttccgtgtat gttgacat	420
aaaaagggaa ccattccat ttccctccc caagaaaatg tctcacaatt acaaagtata	480
aaaacagccg ttcataaatg caaaaaaaaaatctgattata tatgaaataa ttcttagatc	540
aattcaacat atttgatgac atttgtag	573

<210> 332

<211> 555

<212> DNA

<213> Homo sapien

<400> 332

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agtaagttat agacttgctg agtttggcat agatagtgcg ctcatttaat ctgtgcctct	180
caaaacttca gaatattagc atattaccac aaataattt tggtaaaact attgagat	240
taaaattttt gaaatcacta ctgttacctg ttatagaaaa tagtgttggc ttatgtat	300
ctctgtgtaa ctggttacat ttgtatgggt gtctatactc aactggat	360
attgatgtaa acatacctat ccagacataa atgctaagta acattttt cttccctccaa	420

ctacataatt ttagctcat cattttcct taatccttc ctaacttgc gcagcagtt	480
gaatttcca gatattatg tttgaacata atggctaga atacatattt gaacatcata	540
gttgtatata tttt	555
<210> 333	
<211> 460	
<212> DNA	
<213> Homo sapien	
<400> 333	
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ttttcttgag gtacctatat aaatttaatc acctgccccca aagtcccttc gtttaggttaa	180
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gaatgctgat catcttatgc agcatactaa aggtgattt actcttaca aaatagagct	300
taagtatcaa cctgatggaa gtttagaaaat taaaaacatt taagtagaat catctcttc	360
tctattttg agatcctgca gcaaaaagcc tcccaaatac acttcaaag ttctgccatt	420
aaggaatgtt gttctcttg taaaattcag agatctttt	460
<210> 334	
<211> 190	
<212> DNA	
<213> Homo sapien	
<400> 334	
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ctgatagaga cctgtgcaga tgtctcttc tgcctccactcatctca ctggatctgt	120
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ggcccaagg	190
<210> 335	
<211> 394	
<212> DNA	
<213> Homo sapien	
<400> 335	
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gccaggcata tattttctca ccaggacaca tggggcagcg gaccctgggt gtcagtaaga	120
acacacccag aatgatataa ccagatattt ttcagtttct aaattaaggc atattcaaaa	180
aattccatgt acaagtttac accactttc taagttatc accaggtat taaaggcagat	240
tcacagatga attactctca gtttaactat atgcaacaac catgccaata actttcttc	300
taaattttgc ataataatgg taaaaaaag tggtagtttta actatcatgt tcacaattgt	360
cattttcaa ggcagtagaa gaccaagaca tttt	394
<210> 336	
<211> 429	
<212> DNA	
<213> Homo sapien	
<400> 336	
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cttaaaatct tgggtttcag aaagacagtt tataccatga ctgcttaatt atccccccaa	120
agaccttctg attgaagtca tgtacagttc agtggcctaa attctctgcc ttttaactt	180
gctttgcaag cctactctga aaataagtta tttagtcaag ttattctcaa agatgtccca	240
gttgccataga aaggatcaaa tggaacattt gacacacata ctcaaaaaaa tgtaactgac	300

ttaaacact ttaacctaat catctgtatc aaactttcta aaaatcaaat ctcaggattg
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 tatgcattt

<210> 337
<211> 373
<212> DNA
<213> Homo sapien

<400> 337

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 atttagaagt cagcatccaa ggtaaaaagaa ttctctgtt gacttgacat cactcccatc 180
 ctctgatact cgccctactct cttctcaaag aagtttagtct ttcccttccag tgaaaatattc 240
 tccataaaagt caaatgggtt ctctactctg aaaaccttgc taaaacccag ttccagcata 300
 agtctgtctg ccacaaaactc aatgtattgc ttcatcagag tgcaattcat cccaatgagt 360
 ttcacaggca agg 373

<210> 338
<211> 366
<212> DNA
<213> Homo sapien

<400> 338

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 ctgcaggcca cctactctatg cacctaattt gaagcgccac cctagcaata tcaaccattt 240
 accttccttc tacacttattc atttcacaa ttcttaattt actgactatc ctagaaaatcg 300
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<210> 339
<211> 319
<212> DNA
<213> Homo sapien

<400> 339

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 agcctaattt tttttttat caattaacgt taaaaatttgc atcaactatt 180
 taatttcatga ggttccatca tattaaaattt taaccctttaag attcaaccgc catgtgctt 240
 tataaaggaa acatTTTta gagacgtctg agctcacttt tacatggtgg tgcctactgc 300
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<210> 340
<211> 278
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(278)
<223> n = A,T,C or G

<400> 340
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 ttccttagcca tgactactn accagacncc tcaacngct tttnatcaat ngnncacatn 180
 actcgaanacn taaatnatgg ctgaatcatc cgctacctnc acgcaatgg cagcctcaat 240
 attctttatg ctgcctcttc ctacacatgc gggcgagg 278

<210> 341
 <211> 400
 <212> DNA
 <213> Homo sapien

<400> 341
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 ggcttc.aaa catcaacccc aacaagacct cggccagcgg gagctgcggc gcccacctgg 120
 tgactctgga gctgcacagg gagggcacca cctgcctgtc cttccagttc gggatgaatg 180
 caagttctag cccgttttc ctacaaggaa ttcagttgaa tacaattttt cctgacgcc 240
 gagaccctgc ctttaaagct gccaacggct ccctgcgagc gctgcaggcc acagtccgca 300
 attcctacaa gtgcaacgcg gaggagcacg tccgtgtcac gaaggcgaaa tcagtcaata 360
 tattcaaagt gtgggtccag gcttcaagg tggaaaggttg 400

<210> 342
 <211> 536
 <212> DNA
 <213> Homo sapien

<400> 342
 aaagaacaat gggaaaaaca agtccgtgtt ctcacagatg ctgtcgatga cattactcc 60
 attgtgact tcttggctgt ctcagagaat cacatttgg aagatgtgaa caaatgtgtc 120
 attgctctcc aagagaagga tgtggatggc ctggaccgca cagctgggtgc aattcgaggc 180
 cgggcagccc gggtcattca cgtagtcacc tcagagatgg acaactatga gcccaggagtc 240
 tacacagaga aggttctgga agccactaag ctgtctcca acacagtcat gcccacgttt 300
 actgagcaag tagaaggcgc cgtgaaagcc ctcagctcgg accctgccc gcccattggat 360
 gagaatgagt ttatcgatgc ttccgcctg gtatatgatg gcatccggaa catcaggaaa 420
 gcagtgcgtga tgataaggac ccctgaggag ttggatgact ctgactttga gacagaagat 480
 tttgatgtca gaagcaggac gacgtccag acagaagacg atcagctgat agctgg 536

<210> 343
 <211> 646
 <212> DNA
 <213> Homo sapien

<400> 343
 aaaacttcta ttcatcaaaa gacataaaga aaacagtcaa gccacagact aggtgtata 60
 tctcaataca tatatccgac aagagaattt catctagaat gtataaagaa tttctatgac 120
 ccaattatag ctatcaggaa tatacaaatt aaaaccaaaa tgaacatca ctacacaccg 180
 attggaatgg taaaaaggaa aaaatactga caacaccaat attgtaaag acaggaggt 240
 ccagaactct cattcattat attcataat tgacaaatat aaaaactgtc atagtagggc 300
 agtcttcctt agaaaggat tggggcatg acagagaaca atattaatct gtccattata 360
 ttcccttaact gtaaaatgga gaccatatgt tccaccagct tcacttggta attatgatac 420
 atggcttata agagactcaa atgactccat ttcatcaact aatatgcct gtcaattcta 480
 cttctaaagt atccccatgtt ctatccaatg tcataccact atcataattt aagtgttcat 540
 aactctctat aatatttcaa taatctaact ggtctcaatg cctgttagtag aaattgcaga 600
 ttgggctccc caatttctgt tccctaggaa ggctgagaaa gctttt 646

<210> 344
 <211> 383
 <212> DNA
 <213> Homo sapien

<400> 344
 cctgcacccc agtataaggg cctccccaggc tgtagtaagaa gctgcttccc ctccctctcat 60
 aggccaagcc tattgtgtga aaccatctca tggcttggt gacgttagacc atttttgaaa 120
 ccgtctcatg gtcttggtga cgtagaccgt ttgcttctt aactccagcc gcggaatgac 180
 attagtggaa ccgggcttagg gaactgctgg aagttcagga tgccaccacc ttgaacacct 240
 aggccagggc tccccaccat gtcccggtt tctttcttcg agagtataga accgttcatt 300
 ctgtcttgt gtcccattcc atctcttgaa aaaatgttagt ctttgaatgt gtgaaaatct 360
 agggacattc aatctagtct ttt 383

<210> 345
 <211> 263
 <212> DNA
 <213> Homo sapien

<400> 345
 cctcccccattc ccctttgctg gtgggaggag ctcgtgtgtct cttggccgc ttactggaag 60
 ggcgttttc agagctgcag ggacagggtg agcagctgaa gggcttaggag ggaagccggc 120
 ccccgctctg cagaagctgc atttcagctg aatctgtgtt tcagcctcag ttgggttgac 180
 cgtagcccc tctccctcccg gatggtcatg tttttgtcac attagagaat aaacagccac 240
 acacacattt ttttttttcc ttt 263

<210> 346
 <211> 132
 <212> DNA
 <213> Homo sapien

<400> 346
 aaatccaaat aaaaaagcat agtctctgca agatttgtt ctttgaattt cttgatattg 60
 taattgatta ttgataactg tcatcatgaa attatctctc aataataaga taaataaaact 120
 agcatatgaa tc 132

<210> 347
 <211> 564
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(564)
 <223> n = A,T,C or G

<400> 347
 cctgggtatc cagggaggct ctgcagccct gctgaagggc cctaactaga gttctagagt 60
 ttctgattct gttctcagt agtccttttta gaggcttgct atacttgtc tgcttcagg 120
 aggtcgacct tctaattgtat gaagaatggg atgcatttga tctcaagacc aaagacagat 180
 gtcagtggc tgctctggcc ctgggttgca cggctgtggc agctgttgcat gccagtgtcc 240
 tctaactcat gctgtcccttg tgattaaaca cctctatctc ctttggaaat aagcacatac 300
 aggcttaagc tctaagatag ataggtgttt gtccctttac catcgagcta cttccataa 360
 taaccactt gcattcaaca ctcttcaccc acctccataa cgcaaggggta tgtggataact 420
 tggcccaaag taactgggtgg taggaatctt agaaacaaga ccacttatac tgtctgtctg 480

aggngagaaga taacagcgac atctcgacca gcctctgcct taaaggaaat ctttattaat 540
cacqtatggc tcacaagata attc 564

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<210> 348
<211> 321
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(321) .
<223> n = A,T,C or G

<400> 348
gcncatgaac anggagcaac ganaagagat gtcgggctaa gggccggga cgggcggcac 60
ccatcctgcn acggaacacn ttcgggtnt ggtttgatt ngttcacctc tgtttatatg 120
canctatttgc ntccctcctcc cccaccccaag nccccaactt catgcttntc ttccgcnctc 180
agccncctg ccctgtctc gcggtagtc antgaccacn gnttcccctg cangagccgc 240
cgggcgtgag acncngaccc tcnnntgcata caccaggccg ggcccnngct ggctcccccn 300
anagacctgt gaaanagctq q 321
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<210> 349
<211> 255
<212> DNA
<213> Homo sapien

<400> 349
ccatgacagt gaaggggctg ttaggaatat caacaccacc gaagcgcaca tagatcacat 60
atgtgcccgg ctggcagct gtgtagaaga tgtcataggt tccatcttca ttctcaatga 120
catcgccctc ggcctcagtg ccatctgggg tcagaaccgt gcaggtcact ttacccttcc 180
cggcagtctt ggcatcaacc acaaagccta cttcttcgcc agtttcaca gtggaggcga 240
ttccaggacc cgttag 255
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<210> 350
<211> 496
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (496)
<223> n = A,T,C or G
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<400> 350
gggcttattn gctcacaaaa tcattcnctt ttggaaactat ggccaattga agctacacac 60
tgaattttt aatacagcat taagttctt tgtgtaaaaa aatcttgtn cncagtaata 120
aaaaaaagata aggcaagatg cattaaacat gaaaccttct ggcttttc ctctgcgtt 180
ttacagagcc actgatgact atctgcaaca aaagagttaa gtttctgatt ttccgtatca 240
agcatcttat gccttgcgtg tggtaagaat tctggccaag caccctgaag gacagatgct 300
ggtgatggnc ttggcactt atgctggcaa actgagcttc tttcccttga gtactttgn 360
aatgtacaag tagaagaagt cacaagtata ggtatggctg gactacgccc gccaccacag 420
caatgaggc taaaagcccc tcaaagnaga agcgnccaga tccagttgac aagataacaa 480
qcacqataqa qgcccc 496

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<210> 351

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<211> 109
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(109)
<223> n = A,T,C or G

<400> 351
ccatagtgaa gcctggaaat gagtgttact gcagcatctg ggctgccanc cacaggaaag      60
ggccaagccc catgtagccc cagtcatactt gcccagcccc gcctcctgg                  109

<210> 352
<211> 384
<212> DNA
<213> Homo sapien

<400> 352
ccttcgagag tgacctggct gcccaccagg accgtgtgga gcagattgcc gccatcgcac      60
aggagctcaa ttagctggac tattatgact cacccagtgt caacgcccgt tgccaaaaga      120
tctgtgacca gtggacaaat ctggggccccc taactcagaa gcgaaggaa gctctggagc      180
ggaccgagaa actgctggag accattgacc agctgtactt ggagtatgcc aagcgggctg      240
cacccttcaa caactggatg gagggggcca tggaggaccc gcaggacacc ttcattgtgc      300
acaccattga ggagatccag ggactgacca cagccatga gcagttcaag gccaccctcc      360
ctgatgccga caaggagcgc ctgg                                         384

<210> 353
<211> 345
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(345)
<223> n = A,T,C or G

<400> 353
ccttggtcag gatgaagtng gctgacacac cttagcttgg ntttgcttat tcaaaagana      60
aaataactac acatggaaat gaaactagct gaagcctttt cttgttttan caactgaaaa      120
ttgnacttgg ncactttgt gcttggagg gccattttc tgcctggcag ggggcaggtta      180
tgtgcccctcc cgctgactcc tgctgtgtcc tgaggtgcat ttcccttgn ncacacaang      240
gccangntcc attctccctc ctttttacc agngccacan cctnnctgg aaaaangacc      300
agnggtcccg gappaaccca tttgngctct gcttggacag canag                         345

<210> 354
<211> 712
<212> DNA
<213> Homo sapien

<400> 354
ccatctacaa tagcatcaat ggtgccatca cccagttctc ttgcaacatc tcccacctca      60
gcagcctgat cgctcagcta gaagagaagc agcagcagcc caccaggag ctccctgcagg      120
acattggga cacattgagc agggctgaaa gaatcaggat tcctgaacct tggatcacac      180
ctccagattt gcaagagaaa atccacattt ttgccccaaa atgtctatcc ttgacggaga      240

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gtctaaagca gttcacagaa aaaatgcagt cagatatgga gaaaatccaa gaattaagag	300
aggctcagtt atactcagtg gacgtgactc tggaccaga cacggcctac cccagcctga	360
tcctctctga taatctgcgg caagtgcggt acagttacct ccaacaggac ctgcctgaca	420
accccggagag gttaaatctg tttccctgtg tttgggctc tccatgcttc atcgccggga	480
gacattattt ggaggttagag gtggggata aagccaagtg gaccataggt gtctgtgaag	540
actcagtgtg cagaaaaggt ggagtaacct cagccccca gaatggattc tggcagtgt	600
ctttgtgtta tggaaaagaa tattgggctc ttacctccca atgactgccc tacccctgcg	660
gaccggcgtc cagcgggtgg gggattttct tgactatga tgctggggga gg	712
<210> 355	
<211> 385	
<212> DNA	
<213> Homo sapien	
<400> 355	
cctcatagcc gtttagcaca gttacagaat gtctgaaggg gacagtgtgg gagaatccgt	60
ccatggaaa ctttcgggtgg tgtacagatt tttcacaaga cttggacaga tttatcagtc	120
ctggctagac aagtccacac cttacacggc tttgcgtatgg gtcgtgacac tggcctgag	180
ctttgtctac atgattcgag tttacctgct gttgggttgg tacattgtga cttatgcctt	240
ggggatctac catctaaatc tttcatagc tttcttctt cccaaagtgg atccttcctt	300
aatggaaagac tcagatgacg gtccttcgct acccacaaa cagaacgagg aattccgccc	360
cttcattcga aggctccag agttt	385
<210> 356	
<211> 347	
<212> DNA	
<213> Homo sapien	
<400> 356	
aatggagata aagaaaagtct cttttgttt ttagatggaa aagaaagcac aagtttttc	60
tacctgtgaa tgaaccttgg tgaccttat gtgccattca tgcagcattt ttgttcatat	120
tggcttagaa ttcaatgtcat gaatatcatt acattttat atctaaccatt cctagtttagc	180
tttgatcaa aatataaaaa atctgataca tgaataacttt gctagattaa tgacttgatc	240
atctttggaa ttagtaggca agacgatttt tacctattat ttctatgtt gggtaatgt	300
taaaactaaa tacagatgat aataattgct atttcacagt gatgttt	347
<210> 357	
<211> 313	
<212> DNA	
<213> Homo sapien	
<400> 357	
aaagtaatca acctctctgt cttccatta gtctggatcg tctaaagatt gttttatattt	60
tagaggctca tccgggtcaga ttttagtcat gtgaaatttc aggccaggcg tgacgtcagc	120
gtggcatttg aaacagctcc atgttgcct tagtgcgttc tgaccgaagc ctgtctgtcc	180
tcagatataa agatgaagcg cagctgtata aagaagagca cctgaggaat cgccagcacc	240
ctcaactgcta ctttcgtac atgatcgcca tcatcaacaa ctgcagacc ttcaaggaaat	300
ccatagtcag ttt	313
<210> 358	
<211> 403	
<212> DNA	
<213> Homo sapien	
<400> 358	

aaaaagaagg	acttagggtg	tcgtttcac	atatgacaat	gttgcatat	tgtgcagtt	60
tcaagtacca	aaacgttcaa	ttgatgatgc	agttttcata	tatcgagatg	ttcgctcg	120
cagtaactgtt	ggttaaatga	caatttatgt	ggatttgca	tgtataatac	agtgcagac	180
agtaatttta	tctaaattac	agtgcagtt	agttaatcta	ttaataactga	ctcagtgtct	240
gcctttaat	ataaatgata	tgtgaaaac	ttaaggaagc	aatgctaca	tatatgcaat	300
ataaaatagt	aatgtgatgc	tgtgcgttt	aaccaaagg	cagaataaaat	aagcaaaaatg	360
ccaaaagg	tcttaattga	aatgaaaatt	taattttgtt	ttt		403

<210> 359

<211> 411

<212> DNA

<213> Homo sapien

<400> 359

aaataaaatac	ttagaacacg	acttggctcc	tacaaggcatc	tggactctag	gtctcagtag	60
tggagtgtct	caccatggg	ccccacgcag	ggacgccacg	gttccctccc	accccggtat	120
caagacacgg	aatcggtgc	cgatggttgg	atcgcaatgc	gcccctttc	tagagcctc	180
ccggccatc	tacaggcagg	atgcggctgg	aaaaaaagaca	actgaaattt	ctcgaagg	240
gatggtcgc	acggttgagg	attctacgtg	gttcttttgg	ttcccttggt	gtgtgtgt	300
gtggaggagg	ccgcggccct	tagatcacct	tcttgagctc	gtcgtacagg	accagcacga	360
aggcgcccc	catgccccgc	aggacgttgg	accacgcacc	cttgaagaag	g	411

<210> 360

<211> 378

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(378)

<223> n = A,T,C or G

<400> 360

cctcttcagg	ggcccgagcc	agggacaggg	ccttggtttc	tttctccctg	gtttctgcct	60
cagctctgtc	cctctcatcc	gcgtatttgg	aagagatgtt	tttctccctg	gttaacaact	120
gatcaaattt	cctctgtttc	ttttccaggt	tggacacacg	ttgcccgtgg	ttgtccaaat	
180caacaaccag	gtcggtccagc	tcctgctgaa	gcctgttctt	gttctttcc	agtttatcat	
aagggccgc	tttctccctg	tactgctggg	tgaggntctc	gttctccctc	tggAACCTCT	300
tcttccctc	ttccagagct	tccacggngc	tggcaaagtc	ctgcagcttc	ttcttcgagt	360
cgagagactg	gtgttga					378

<210> 361

<211> 372

<212> DNA

<213> Homo sapien

<400> 361

aaatactggg	ggcattaaag	agtggatgta	gtcaagagct	tagctaacat	tgcctttca	60
ctctatTTT	ctcagatatt	gttaaggatTC	tgtttttcaa	tattgtatTT	atTTTTTGG	120
cttcaacag	cagccctagt	aatgggtggag	ttgttaatta	atgtgtatAT	tgtactgaat	180
ttctgtcagt	taaggggttc	actgcttgg	tggaaattgg	tggaaattgc	tagcagg	240
cacgatgtt	atTTTTTCT	ccatgttgta	tatcattacc	atTCcacata	cgcgtttct	300
tttttctcc	tctccctctg	atctccctaa	aaatgaatct	agagttgg	gtttttccc	360
cctcccttt	gg					372

<210> 362
 <211> 544
 <212> DNA
 <213> Homo sapien

<400> 362

cctgagtcac	ctagcatagg	gttgcagcaa	gccctggatt	cagagtta	aacagaggct	60
tgc	cccttc	aggacaacag	ttcaattcc	aaggagccta	cctgaggtcc	120
tgggtcccc	aggataaaa	cgacaatgtg	ccttttatt	attatttatt	tggtggtcct	180
gtgttatta	agagataaa	tgtataacca	cctagctctt	ttcacctgac	tttagtaataa	240
ctcataactaa	ctgttttgya	tgccctgggtt	gtgacttcta	ctgaccgcta	gataaacgtg	300
tgcctgtccc	ccaggtgggt	ggaataattt	acaatctgtc	caaccagaaa	agaatgtgtg	360
tgtttgagca	gcattgacac	atatctactt	tgataagaga	cttccctgatt	ctcttaggtcg	420
gttcgtggtt	atcccattgt	ggaaattcat	cttgaatccc	attgtcctat	agtccctagca	480
ataagagaaa	tttcctcaag	tttccatgtg	cggttctcct	agctgcagca	atactttgac	540
attt						544

<210> 363
 <211> 328
 <212> DNA
 <213> Homo sapien

<400> 363

aaactggta	tgacaaaagc	cttttagttgt	gtttcttgaa	ctataaagaa	aacaaatttt	60
ggcagtc	ttt	aagtatata	agcttaaat	ataatttta	gcatttggca	120
gccattat	at	ttgatttgc	attactgtt	cacaatgaag	ctttctttaa	180
tttatgatta	tga	aaagaaat	aaggcacaac	cacagtttt	ctttcttaaa	240
gtttagtgtg	ttc	tttttgtg	ttaaaaaaaaaa	aaagtgcac	tatcaaaact	300
agagtaat	at	tgccgttctg	ctgatttt			328

<210> 364
 <211> 569
 <212> DNA
 <213> Homo sapien

<400> 364

cctgggcacc	tcttgcttg	aaatatggca	agacttggaa	aaatgttgc	ccttagaaatc	60
tatctca	cta	tttagtttag	ttgtctc	ttggcctggg	cacagttctg	120
ggaacagact	ccctttcta	aaactgaact	tgaccacatc	aaaagttgt	aaaacaatct	180
ccatggtaat	taaaacttgca	ttcaacacca	tatggtaaca	gaagatggca	aaggataaga	240
ttcagatctt	agatcttcc	aagttagggca	tgttagatga	tagaaggatt	agttgcac	300
tggatctgag	ctcaggctt	ggcatgaagg	aaactgtctc	ccatgtggtt	tggaaagagt	360
aggggctccc	ttagctctat	tgtgaactat	acgggttca	tccaaggaat	ggtatgtat	420
gggcataaaaa	ccattctca	gacaactgaa	gatggtcccc	ttctgttagcc	agaaacacta	480
gctgtcctgc	attgtccatt	tccttagcc	ccaggcggtc	ctgtgtgtac	agggaggtct	540
cctgtaaagg	aatggttcc	ttggcttgg				569

<210> 365
 <211> 151
 <212> DNA
 <213> Homo sapien

<400> 365

aaaaaaaaaa	atc	tttttat	tatggat	ttt	gtcaaacaca	cacacaagca	taacaaaccc	60
------------	-----	---------	---------	-----	------------	------------	------------	----

ctaggtaccc atctccaagt tttgaccctt attataattt catcttcagt gttttattat	120
ccacttcctc tctctctatc ttttagtattt t	151
<210> 366	
<211> 508	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(508)	
<223> n = A,T,C or G	
<400> 366	
agtataaaga tatattccat aaaagagttt ggcagtcaaa ganaagcatc gcacttccga	60
aaaacacaag cattttctc ctatgttaca gagaatttngn taaaaaaaaaaa aaaaaatcat	120
catcaacagc cnccantnta cnccacacta gaatgtacac tccggcaagt aaattaagggn	180
tgcagtccat ccctgaacga tganaagnnn tctgagctat ggcaaagngt tanaaagttag	240
cccagctana caaatgcccc agctatcccc aggggagttt ttcaagtactt aanacttcat	300
ttccaananc agccccggaa aagccctgac aggaaggggg gaccagngat caccgatntc	360
ccatttagggg cggnncaccaa aaacaaaatg cctggagctt ntgagcagct gcagcctggg	420
gttgtggcta ggcncngggn gnggttgcaa aaaaacggct gtntccgggg agaggcaaatt	480
ggcaggccag ccagccctgg gtacatgg	508
<210> 367	
<211> 382	
<212> DNA	
<213> Homo sapien	
<400> 367	
cctgagccgc tagtctttaa gatgcgttcc tatcgtttgc tgcaaattccg agcagaagcc	60
ctcctggccgg caggcagcca tgtgatcatt ctgggtgacc tgaatacagc ccacccggccc	120
attgaccact gggatgcagt caacctggaa tgctttgaag aggaccagg ggcgaagtgg	180
atggacagct tgctcagtaa cttgggtgc cagtctgcct ctcatgttagg gcccttcatc	240
gatagctacc gctgcttcca accaaagcag gagggggccct tcacctgctg gtcagcagtc	300
actggccccc gccatctcaa ctatggctcc cggcttgact atgtgctggg ggacaggacc	360
ctggtcatac acacctttca gg	382
<210> 368	
<211> 174	
<212> DNA	
<213> Homo sapien	
<400> 368	
ccttctccct ctttgacaag gatggagatg gcactatcac caccaaggag ttggggacag	60
tgtatgagatc cctggacag aacccactg aagcagagct gcaggatatg atcaatgagg	120
tggatgcaga tggaaacggg accattgact tcccgagtt cctgaccatg atgg	174
<210> 369	
<211> 216	
<212> DNA	
<213> Homo sapien	
<400> 369	
aaatctcatg gtttcttata aaaaaatata tatatagggc cccaatccat tgccatcaa	60

ttgcccttgg actttccaa ggtatattat ggggtttat gcaaaattcc aagctaccat	120
gtaactttt ttaaccattt aacaaggagg ggaactgtt tcctaccttc tttacatgtt	180
gtgcattgtt gtggtccaga aatgccaaac cttttt	216

<210> 370
<211> 344
<212> DNA
<213> Homo sapien

<400> 370	
ccttggtcag gatgaagttg gctgacacag cttagcttgg tttgtttat tcaaaagaga	60
aaaataactac acatggaaat gaaacttagct gaagcctttt cttgttttag caactgaaaa	120
ttgtacttgg tcactttgt gcttgaggag gcccatttc tgccctggcag ggggcaggc	180
tgtccctcc cgctgactcc tgctgtgtcc tgaggtgcat ttccctgttgc acacacaagg	240
gccaggctcc attctccctc cctttccacc agtgccacag cctcgctgg aaaaaggacc	300
aggggtccc gaggaaccca tttgtgctct gcttggacag cagg	344

<210> 371
<211> 741
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(741)
<223> n = A,T,C or G

<400> 371	
aaattacata tctaatttgt tgatttgtt aatgccatt tcttcatcta agtgctaagt	60
gctaagtgtt gcagttgtt ccctgctaca ctccaaggca caaaggagtt caaggaatgt	120
gcaatggaaa tcagtttagat gaatgtgtt ggaaccttcc cttaataaaa gctggatccc	180
acactagccc ctacaccctc tcatacccaa atattctgc ttccctctac ctgcacttgc	240
tgttctctcc tctgccacac aaatctacct ctcaagccta ggtcccaccc gcttcatgac	300
aactttccag actattccag aaccttaac catctctgac ctctcatcag atctatgttgc	360
tacataaacac caattaatga gatcattact gctttatgtt ctaattgtt cctgtattca	420
aaatcttctc tccaaccaca taatgactcc ctaaacttct cttgtatccc ccaatgcctt	480
gtacaagcac agaactggtc aatcaataaa tactcactgg ttatttgagg aaaaaatgtt	540
gccaagcacc atcttatca gaaaataaat caattcttct aaacttggag aaatcacccct	600
atcccttagta tgtatcttta attagaacaa ttcagattga gaangngaca gcatgctggc	660
agtcctcaga gccctcgctt gctctcgna cctccctgcc tgggctccca ctttggtggc	720
atttgaggag cccttcagcc t	741

<210> 372
<211> 218
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(218)
<223> n = A,T,C or G

<400> 372	
ccgccagtgt gctgaaattc gcccttggcc gcccgggcag gtaccacaac agcaggncgt	60

agtgagaaat ctaccacctt ctacagtagc cccagatcac cgacacaac actctcacct	120
gccagcacga caagctcagg cgtcagtcaa gaatccacca cctccacag ccgaccaggc	180
tcaacgcaca caacagcatt ccctggcagt accttgggn	218
<210> 373	
<211> 168	
<212> DNA	
<213> Homo sapien	
<400> 373	
actgctaggg aatgtgtttg tgcattga gcctggcg ctgtggagg ttgtggattc	60
ttcactgacg cctgagcttg tcgtgctggc aggtgagagt gttgtgtccg gtgatctggg	120
gctactgttag aaggtggtag atttctcact cagggctgct gttgtgg	168
<210> 374	
<211> 154	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(154)	
<223> n = A,T,C or G	
<400> 374	
tgagaaatct accacccctt acagngagcc ccanatcacc ggacacaaca ctctcacctg	60
ccagcacgac aagctcaggc gtcagtgaag aatccaccac ctcacacagc cgaccaggct	120
caacgcacac aacagcattc cctggcagta cctc	154
<210> 375	
<211> 275	
<212> DNA	
<213> Homo sapien	
<400> 375	
actgccaggg gacagtgtcg tgcaggtaa acctggctg ctgtggaaag ttgttgattc	60
ctgactgggg cctgagggtgg tgggtgtggc aggtAACAGT gttgttatccg ttgagcctgg	120
gctgctgtgg gaagttgttag aatGCCACT gaggcctggc gtgggtgtgc tgcaggaa	180
tgctgttgtg tgcgttgagc ctggcggct gtggagggtg gtggattctt cactgacgcc	240
tgagcttgtc gtgctggcag gtgagagtgt tgtgg	275
<210> 376	
<211> 191	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(191)	
<223> n = A,T,C or G	
<400> 376	
actgccaggg gacagtgtcg tgcaggtaa acctggctg ctgtggaaag ttgttgattc	60
ctgactgggg cctgagggtgg tgggtgtggc aggtAACAGT gttgttatccg ttgagcctgg	120
gctgctgtgg gaagttgttag aatGCCACT gaggcctgccc gtgggtgtgc tgntaggaa	180

191

tgctgcttagc g <210> 377
 <211> 476
 <212> DNA
 <213> Homo sapien

<400> 377
 ccggccagtgt gctggaattc gcccttggcc gcccgggcag gtacatttc ttgttagactc
 tggtaatttc ctgcagctcc tggttggttc tggagcagat gatctaattg agagagtct
 cgtcggttcc cagccccttc atgaaagctt ttagctcaga agcgtcatac tgaggcagg
 tcttcataatg gccaaaatc accgtctcca ggtggccaga taaggctgac ttcaatgt
 atgcaagttc cttttggtc cttctgtgtt aggcaaggc aatatcctgt ctctgtcat
 tgctcggtt ggtcaaaaatg ttgacaatgg tgacccatc cacacccctt gtcattgt
 ctgttcaat gtcataagca tcccgtctcag catcaaaatg agtataaggct ttgacagacc
 catatgcact tgggggtgta gagtgatcac cctccaagcc gagcttgacaggatt
 60
 120
 180
 240
 300
 360
 420
 476

<210> 378
 <211> 455
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (455)
 <223> n = A,T,C or G

<400> 378
 agtgtgctgg aattcgccct tggccgccc ggcaggta catcccatct tcaaattt
 aatcatattt tcagttgtcc aaagcagctt gaatttaaag tttgtgctat aaaattgt
 aaatatgtta aggttggaa cccaccaatg cactactgtt atatccgtt tcctaaattt
 ctccaccta cagataatag acaacaatg tgagaaaacta aggctaacca aacttagata
 taaatcctac caataaaaatt tttcagttt aagttttaca gtttatttaaa acaaaaaac
 agaaacaaat ttcaaaataa atcacatctt ctcttaaaac ttggcaaaacc ctcccttaac
 tgtccaagtn tgagcataca ctgccactgg ctttagatac tccaattttaa tgcactactc
 tttcactggc ctgaatgaag tatggtaaaa caagc
 60
 120
 180
 240
 300
 360
 420
 455

<210> 379
 <211> 297
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (297)
 <223> n = A,T,C or G

<400> 379
 agctcggttcc cctagnacgg ccggccagtgt gctggaattc gcccttagcg gcggccgg
 caggtaaaa gaatccttag acgcataact gagtttaag ttccttaatt cctaattt
 ggcttctgtt gaagcctcct cacagtaggc ttcacttaggc ccacagtgc cctagacactc
 tgacaatccc accctagaca gactttattt caaaaatgcgc ctgaagaggc agatgattcc
 caagagaact caccaaatca agacaaaatgt cctagatctc tagtgtggna gaactat
 60
 120
 180
 240
 297

<210> 380

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<211> 144
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(144)
<223> n = A,T,C or G

<400> 380
actttgtga aaatctttt tcccagggtc tataaaacat taatttgttt ttatattta      60
ctatttttt gngttttttt gtttttaat caataagtaa tctaggacta gcattatgtt      120
tgctagacct ggcatttgct cggc      144

<210> 381
<211> 424
<212> DNA
<213> Homo sapien

<400> 381
actcttgaat acaagtttct gataccactg cactgtctga gaattccaa aacttaatg      60
aactaactga cagttcatg aaactgtcca ccaagatcaa gcagagaaaa taattaattt      120
catgggacta aatgaactaa tgaggataat atttcataa ttttttattt gaaattttgc      180
tgattctta aatgtcttgc ttcccgatt tcaggaaact tttttctt taagctatcc      240
acagcttaca gcaatttgat aaaatatact ttgtgaaca aaaattgaga catttacatt      300
ttctccctat gtggtcgctc cagacttggg aaactattca tgaatattta tattgtatgg      360
taatatagtt attgcacaag ttcaataaaa atctgctct tgtataacag aatacatttgc      420
aaaa      424

<210> 382
<211> 408
<212> DNA
<213> Homo sapien

<400> 382
actcttgaat acaagtttct gataccactg cactgtctga gaattccaa aacttaatg      60
aactaactga cagttcatg aaactgtcca ccaagatcaa gcagagaaaa taattaattt      120
catgggacta aatgaactaa tgaggataat atttcataa ttttttattt gaaattttgc      180
tgattctta aatgtcttgc ttcccgatt tcaggaaact tttttctt taagctatcc      240
acagcttaca gcaatttgat aaaatatact ttgtgaaca aaaattgaga catttacatt      300
ttctccctat gtggtcgctc cagacttggg aaactattca tgaatattta tattgtatgg      360
taatatagtt attgcacaag ttcaataaaa atctgctct tgtatgc      408

<210> 383
<211> 455
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(455)
<223> n = A,T,C or G

<400> 383
actcttgaat acaagtttct gataccactg cactgtctga gaattccaa aacttaatg      60

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aactaactgn cnncttcatg aaactgtcca ccaagatcaa gcagagaaaa taattaattt	120
catggacta aatgaactaa tgaggataat atttcataa ttttttattt gaaattttgc	180
tgannctta aatgtctgt ttcccagatt tcagggaaact ttttttctt taagctatcc	240
acagcttata gcaatttgat aaaatatact tttgtgaaca aaaattgaga catttacatt	300
ttctccctat gtggcgctc cagacttggn aaactattca tgaatattt tattgtatgg	360
taatatagtt attgcacaag ttcaataaaa atctgcttt tgtataacag aatacatttg	420
aaaacatgg ttatattacc aagacttga ctaga	455
<210> 384	
<211> 376	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(376)	
<223> n = A,T,C or G	
<400> 384	
actcttgaat acaagggttct gatatcaactg cactgtctga gaatttccaa aactttaatg	60
aactaactga cagttcatg aaactgtcca ccaagatcaa gcagagaaaa taattaattt	120
catggacta aatgaactaa tgaggataat atttcataa ttttttattt gaaattttgc	180
tgattctta aatgtctgt ttcccagatt tcagggaaact ttttttctt taagctatc	240
cacagcttac agcaatttga taaaatatac ttttngaaac aaaaatttag acatttacat	300
tttctcccta tggggcgct ccagacttgg gaaactattc atgaatattt atattgnatg	360
ggaatatagc attgcc	376
<210> 385	
<211> 422	
<212> DNA	
<213> Homo sapien	
<400> 385	
acctgtgggt ttattaccta tgggttata tcctcaaata cgacattcta gtcaaagtct	60
tggtaatata accaatgttt tcaaatgtat tctgtcatac aaagagcaga tttttattga	120
acttgtcaa taactatatt accatacaat ataaatattc atgaatagtt tcccaagtct	180
ggagcgacca catagggaga aatgtaaat gtctcaattt ttgttcacaa aagtatattt	240
tatcaaattt ctgtaagctg tggatagctt aaaaagaaaaa aagttcctg aatctggga	300
aacaagacat taaaagaatc agcaaaaattt caaaataaaaa attatgaaaa tattatcctc	360
attagttcat ttagtccccat gaaattaattt attttctctg cttgatcttg gtggacagtt	420
tc	422
<210> 386	
<211> 313	
<212> DNA	
<213> Homo sapien	
<400> 386	
caagtaggtc tacaagacgc tacttccct atcatagaag agcttatcac ctttcatgtat	60
cacgcctca taatcatttt ctttatctgc ttccctgtcc tttatgcctt tttccataaca	120
ctcacaacaa aactaactaa tactaacatc tcagacgctc aggaaataga aaccgtctga	180
actatcctgc cccatcat cttatgcctc atcccttcc catccctacg catccttac	240
ataacagacg aggtcaacga tccctccctt accatcaaattt caattggcca ccaatggtag	300
tgaacctacg agt	313

<210> 387
 <211> 236
 <212> DNA
 <213> Homo sapien

<400> 387
 cgcctcata atcattttcc ttatctgctt cctagtcctg tatgccctt tcctaacact 60
 cacaacaaaa ctaactaata ctaacatctc agacgctcag gaaatagaaa ccgtctgaac 120
 tattcctgccc gccatcatcc tagtcctcat cgccctccca tccctacgca tcctttacat 180
 aacagacgag gtcaacgatc cctcccttac catcaaatca attggccacc aatgtt 236

<210> 388
 <211> 195
 <212> DNA
 <213> Homo sapien

<400> 388
 acggcccttt cctaacactc acaacaaaaac taactaatac taacatctca gacgctcagg 60
 aaatagaaaac cgctctgaact atcctgccccg ccatcatcct agtcctcattt gccctcccat 120
 ccctacgcat cctttacata acagacgagg tcaacgatcc ctcccttacc atcaaatcaa 180
 ttggccacca atgtt 195

<210> 389
 <211> 183
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(183)
 <223> n = A,T,C or G

<400> 389
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 cctgaactat cctgcccccc atcatcctag tcctcatcgc cctcccatcc ctacncatcc 120
 ttacataaac agacgagggtc aacgatccct cccttaccat caaatcaatt ggccaccaat 180
 ggt 183

<210> 390
 <211> 473
 <212> DNA
 <213> Homo sapien

<400> 390
 acaaaggcgc aactgcaata ctcaaggtaa aacattaga aaagcatttg tgtgacaggt 60
 atattacagt attatcaaaa tattacattt tcagacttac ttagcagata atcatccacc 120
 agagcttaaa tctttaattt atttccatag tcttaaaaaa tatgtatgt cagaatgcatt 180
 ataaaaagaa tgtaaaagga aacctaaaat acaaatggaa taatgtaa aataaaatattt 240
 tgatttcagt aactgttaat aatcagctca acaccaccat tctctctaa ctcattttaa 300
 ttcttatagg aataatgaac tgtcaaatgc catggcataa ttattttttt ccaagctatc 360
 atcaatgatt agaactaaaaa aaaatttggc ataaaaaaat cacaattcag cataaataaa 420
 gctattttta gcttcaacac tagctagcat ctctaaagaat tgttcaaata agt 473

<210> 391
 <211> 216

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<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(216)
<223> n = A,T,C or G

<400> 391
atttgtattt taggttcct tttacattct ttttatatgc nntctgacat tacatattt      60
ttaagactat gcaaataatt taaagattt agctctggtg gatgattatc tgctaagtaa     120
gtctgaaaat gtaatatttt gataatactg taatataccct gtcacacaaa tgctttctc     180
atgttttaac cttgagtatt gcagttgctg ctttgt                         216

<210> 392
<211> 98
<212> DNA
<213> Homo sapien

<400> 392
acttatttca acaattctta gagatgctag cttagtggta agctaaaaat agctttattt      60
atgctgaatt gtgattttt tatgccaat ttttttaa                           98

<210> 393
<211> 397
<212> DNA
<213> Homo sapien

<400> 393
tgccgatata ctctagatga agtttacat tggtgagcta ttgctgttct cttggaaact      60
gaactcaatt tcctccttag gctttggatt tgacattgca tttgaccctt tatgttagtaa     120
ttgacatgtg ccagggcaat gatgaatgag aatctacccc cagatccaag catcctgagc     180
aactcttgat tatccatatt gagtcaaattt gtaggcattt cctatcacct gtttccattc     240
aacaagagca ctacattcat ttagctaaac ggattccaaa gagaattt gcatggaccg     300
cgactaattt caaatgctt tttatttta ttatttta gacagtctca ctttgcgcc     360
caggccggag tgcaatggtg cgatctcaga tcagtgt                         397

<210> 394
<211> 373
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(373)
<223> n = A,T,C or G

<400> 394
ttacattgtt gagctattgc tggttcttgc ggaactgaac tcactttcct cctgaggctt      60
tggatttgc attgcatttgc acctttatgc tagtaatttgc catgtgccag ggcaatgtt     120
aatgagaatc taccggcaga tccaaacatc ctgagcaact cttgattatc catattgtt     180
caaatggtag gcatttgc tccacgtttt ccattcaaca agagcaatc attcattttt     240
ctaaacggat tccaaagagt agaatttgc tggaccacgac tantttcaaa atgctttta     300
ttatttattt ttttagaca gtctcactttt gtcggccagg ccggagtgca gtgggtcgat     360
ctcagatcgttgtt                         373

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<210> 395
<211> 411
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(411)
<223> n = A,T,C or G

    <400> 395
actgatcatt ctatccccc ctctattgtat ccccacctcc aaatatctca tcaacaaccg      60
actaatcacc acccaacaat gactaatcaa actaacctca aaacaaatga taaccataca      120
caacactaaa ggacgaacct gatctttat actagtatcc ttaatcattt ttattgcac      180
aactaacctc ctggactcc tgcctcactc atttacacca accacccaat tatctataaa      240
cctagccatg gccatccccct tatgagcggg cgcaagtattt ataggcttc gctctaagat      300
taaaaatgcc cttagccact tcttacngca aggcacaccc acacccctta tccccatact      360
agttattatc gaaaccatca gcctactcat tcaaccaata gccctggccg t      411

    <210> 396
    <211> 411
    <212> DNA
    <213> Homo sapien

    <400> 396
actgatcatt ctatccccc ctctattgtat ccccacctcc aaatatctca tcaacaaccg      60
actaattacc acccaacaat gactaatcaa actaacctca aaacaaatga tagccataca      120
caacactaaa ggacgaacct gatctttat actagtatcc ttaatcattt ttattgcac      180
aactaacctc ctggactcc tgcctcactc atttacacca accacccaac tatctataaa      240
cctagccatg gccatccccct tatgagcggg cgcaagtattt ataggcttc gctctaagat      300
taaaaatgcc cttagccact tcttaccaca aggcacaccc acacccctta tccccatact      360
agttattatc gaaaccatca gcctactcat tcaaccaata gccctggccg t      411

    <210> 397
    <211> 351
    <212> DNA
    <213> Homo sapien

    <220>
    <221> misc_feature
    <222> (1)...(351)
    <223> n = A,T,C or G

    <400> 397
ngccgangta caaaaaaaag cacattccta gaaaaaggta ttggcaaata gtaaaaatgg      60
gaggtcaaaa ncaaaaaaaaaa aaaaaacaaa acaaaaaaaaa gaaaaaaccatca acaattttc      120
aattcagtgt gcaaacatta tataaaaata gaaatactaa ctctacaggc agtattttct      180
gataaaattat taaaatagca tatctacnca atctgagata tctattccaa tggcaatgag      240
aaaataattt ataaaaataa agcaatggta taccanatga tagaaaaaaaaa cataactttc      300
agaaatttgta tttaacattt caatgttattt tccttattgn gaatncttct c      351

    <210> 398
    <211> 363
    <212> DNA

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<213> Homo sapien

<400> 398

acaaaaaaaaaa	gcacattcct	agaaaaaggat	attggcaaat	agtaaaaatg	ggaggtcaaa	60
agaaaaaaaaaa	aaaaaaaacaa	aacaaaaaaaaa	agaaaaaaacc	aacaattctt	caattcagtg	120
tgcaaacatt	atataaaaat	agaaatacta	actctacagg	cagtattcc	tgataaaatta	180
ttaaatagc	atatctacac	aatctgagat	atctattcca	atggcaatga	gaaaataatt	240
tataaaaata	aagcaatggt	ataccagatg	atagaaaaaa	acataacttt	cagaatttgt	300
attnaacatt	tcaatgctat	ttccttattt	ggaatacttc	tctgcagagt	ttttatgcta	360
tgt						363

<210> 399

<211> 360

<212> DNA

<213> Homo sapien

<400> 399

actgtttcct	cgtggttcag	gggtgtgcat	gaaggcttt	aggagagcaa	acacctgttc	60
ctattctgt	tgccctccc	tcatttcaa	tgagagtaac	caatttagta	aaataaccaa	120
ataaccatt	ccccaccatg	aacatgggc	ttgggaagac	agtcctacaa	tcttcatcat	180
atatttaggt	ttttaggcca	gccagcttt	tttttccaaa	gctttttttt	gaataccgc	240
ccggccggcc	cctaaggcg	aattctgcag	atatccatca	cactggcgcc	cgctcgagca	300
tgcatctaga	ggcccaatt	cgccctata	tgagtcgtat	tacaattcac	tggccgtcgt	360

<210> 400

<211> 87

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(87)

<223> n = A,T,C or G

<400> 400

ctgcacatat	cnattacact	ggcgccgct	cgagcatgca	tgnagagggc	ccaattctcc	60
ctatatttag	tggaattaca	atncnct				87

<210> 401

<211> 328

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(328)

<223> n = A,T,C or G

<400> 401

acccagggac	acaaacactc	tgcctaggaa	aaccagagac	ctttgttac	ttgtttatct	60
gctgaccc	cttccactat	tgtccatga	ccctgc	aaaaacac	ccatctctg	120
ccaagaatga	tcaataaaaa	ataaaat	aaaaaaa	aaaaaaa	agagaggaac	180
ccacaaaaaa	aaaaaaaag	aaagtntata	aaataaaaata	ttgaagtcc	ttccat	240
aaaaaaaaaa	aagaaaaagc	acggactt	tcatccagtt	ctgatgtgat	tatctctgga	300
aggcattt	tcctcctt	ccctcccc				328

<210> 402
 <211> 268
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (268)
 <223> n = A,T,C or G

<400> 402

nacataatga caacatcttc actagactga gtgttcaagg atttgagatg attcgctatt	60
catcacaccc cgaagattga gatccactgt atttacacaa agcaaagcca tgcagcaag	120
ggactgtcaa cctgattctg agaacataaa cattcaaaaat ttatttcca gtgttcctt	180
ttggaaacca acaacacatc tttaataacct acacacacac acatctntac cttaaaaaaa	240
aaaaaaaaaaag tgnaacttca cagatag	268

<210> 403
 <211> 538
 <212> DNA
 <213> Homo sapien

<400> 403

acagtgtatgc tccccctgg gcaataacaat acaagaacag tgggttttgt caaatggaa	60
caagggaaaca gaaccacaga aataaaataca ttggtaaca tcagattagt tcaggttact	120
ttttgtaaa agttaaagta gaggggactt ctgtattatg ctaactcaag tagactggaa	180
tctcctgtgt tctttttttt tttaattgg tttaatttt tttaattgg atctatcttc	240
ttccttaaca ttccatgtgg agtatgttagc atttagcacc actggctcaa tgcgctcacc	300
taggtgagag tgtgaccaaa tcttaagca ttatgtctat tatcagttac caccatttg	360
ggcttttata cttcatgggt tatgtatgttc tctgtatgac acatttctct gagttttgt	420
attccagcca aagagagacc attcactatt ttagggctgg ctgcgtcag acatttaaag	480
cttttagaga atacactaca ccagggagta tgactactag tatgactatt aggagggt	538

<210> 404
 <211> 310
 <212> DNA
 <213> Homo sapien

<400> 404

tttttttata gataacaattt gcttttattt gtgattcatg agtcagggca gtttccattc	60
tgcaaaatat agttagatgt cctactggc aataacaacag tagaacatgt gttttgtaa	120
aatgggaatc caggaacaga agaatataaa taaattgtatt taaataaaact gattggtaa	180
tttcagaata cttcatatata ctttttcta agattnaaag cagaaaggac tttcttactg	240
tgctgactca gacagcctgg actctcatgt ttttagaaaa attttgtctg ttctggatc	300
tacctgcttc	310

<210> 405
 <211> 559
 <212> DNA
 <213> Homo sapien

<400> 405

acaatcaca attattaact cactggtagg gcagtgtatga tcaaaaccaat tgcattcatc	60
catgctgtaa tggactaaa ggctgactgc agccggcaaa aaagaatgt	120

agtatgaatt tataaaaaca ttttagatgg ctgacaacgg atcttatttt taaagaatat	180
gtctaattca gaggatcgac aactaatcca ttcaataaaa acaatgggga attttttatt	240
gaataaaaat gtaatatgca taaaaactca agaaggctt taaaaatac ttcccccac	300
atcattatcc catacttcat gctaatttt aaaagaatct tgaaatctt aaaaacaagat	360
gaagagaatc ttgttttaag tgacaagttt acattattcc tatattaaat gtcaaactgc	420
tattaatgag tagaagttagg aacaaacccg gatcttagga tcctgtccag ggctcattcc	480
ataactccta tattcacaaag acaagatctg gaaccagaaa acagtcatca tccaatgtgc	540
atcagccttg cgcaacag	559

<210> 406
 <211> 427
 <212> DNA
 <213> Homo sapien

<400> 406	
acaacagaat atctcgggaa tggactcaga agtatgccat gtgatgctac cttaaagtca	60
gaataaacctg cattatagct ggaataaaact ttaaattact gttccctttt tgattttctt	120
atccggctgc tccttccatca gacctcatct ttttaattt tatttttgt ttacccctt	180
ccatttcatc acatgctcat ctgagaagac ttaagttctt ccagcttgg acaataactg	240
cttttagaaa ctgtaaagta gttacaagag aacagttgcc caagactcag aatttttaaa	300
aaaaaaaaatg gacatgtgtt attatgtggc caatgtctt actctaactt gtttatgaga	360
ctaaaaccat tccttactgc tctaacatgc tgaagaaatc atctgagggg gagggagatg	420
gatgctc	427

<210> 407
 <211> 419
 <212> DNA
 <213> Homo sapien

<400> 407	
acaatttgc gttttggcta ataatcatc cttaacctag aattcagatg	60
atcctggaat taaggcaggc cagaggactg taatgataga attaaattag tgtcaactaaa	120
aactgtccca aagtgcgtc tcctaatagg aattcattaa cctaaaacaa gatgttacta	180
ttatatcgat agactatgaa tgctattctt agaaaaaagtc tagtgcacaa tttgtcttat	240
taaataaaaaa caatgttagga gcagcttgc ttcttagttt atgtcattta agaattacta	300
acacagtggc agtgttaaat gaagatgctg tctacaaggt agataatata ctgtttgata	360
ctcaaaacat ttttcatat ttttaaagta gaagttacat aattctatat ttttaagtct	419

<210> 408
 <211> 523
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(523)
 <223> n = A,T,C or G

<400> 408	
acatttgc ttatgtgaat gttgagttt tttcttctaa ttttcaatcc agcagtgttt	60
agggtttca gatgccttat tccagtgtga acagaaaaag ttcataattt atgtggttaa	120
tgctttgatg tgcacatata agatgtttt gtagaaaaatg ttggcacaat tttaacttct	180
tagtggcttgc tgacattata tattatata atatgtatata atatctttt aacattctg	240
tgtttagtag tggaaatgtt ctggcaagt tttaatattt tgaatgcctt tggatattcc	300
agcaataaaag gcatcatgtt ctgcaatagg atttcttact catttaccta tttaacact	360

aaaatagacc acaaactgagc acaaattcct tttataaaatg ttatagaagg aggaaagaat	420
aataaacaca ttgtgaatt gtggtcagt ttatattatct ttaggaaagg ctgatcattt	480
atcttatagc acataacccc agcctcttat tcattatggn taa	523

<210> 409
<211> 191
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(191)
<223> n = A,T,C or G

<400> 409	
accccgtagt gatgagcaact gactggttca ctggccacat tttagttctt cataataata	60
ggccacaaaaa gggctctgtg gttgcctcc atgtgcactg gcccccccc accccttaggg	120
ggcactcaagt agctgctgag aaggcctgtc cacgangctg ttgaaacccc ttcaataaat	180
acttagaagn a	191

<210> 410
<211> 403
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(403)
<223> n = A,T,C or G

<400> 410	
acactggcca gtgtgtttt ggcgattaaa cataatcctg tgaatcagat taattcactt	60
gctgagtggtt catttgcggc atccctctgt tgggtcttgg gggccctcca cgacctcg	120
gggctccccg tggccactc tgcccagagc ctcgcttgaatttctgctgatccatccc	180
gttatagcc agagtaatcc cggggagac tgaactgaga ctgtgtataa ccactgttt	240
gagtgttaga gaatgaaggg cggtaaccat catatcctcc tctgaatcca ttggcagg	300
cccggtatcc attcatcaag cctctagcac cacgggagcc tccacgagac acaccacgac	360
tattgtataa gggctgattt ctacgtggaa atccagtgnctg	403

<210> 411
<211> 384
<212> DNA
<213> Homo sapien

<400> 411

acgtgaaatc ataacaacat gttctcttgtt gttggcttc tcttgcttag catgatattt	60
ttacgggtca cccatattgc atgtatcagg aatataatcc ttttattat ttagttagtgt	120
tctattgtat gtatatacca cagtttattt ctcccttcat cctttgttag attttgggt	180
tttttcacat tgcgttattc aagtataaac ctgctctcaa cattcatgtg caagtcttt	240
agtggacata tatttgcgtt ttctcttgag tgaatgcacc ttgtgggtc acgtggctt	300
atttaaaaaa atttaatca ctgtggtgca tatgttagtga ttattagtga ttatctcata	360
attttatattt ctgtatgact aatg	384

<210> 412
<211> 315

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<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(315)
<223> n = A,T,C or G

<400> 412
acaatatttc tccttgaga agataggata tatgatttc ccaaaaatca caactttgaa      60
ggaagactta nttgctgact tcaattatat cctggactg gcaacttgtg cccttcctt     120
gcttcaaaaa aagtgtaga aagagtgata agatcaactt taatcattct tggatcttca     180
gcaaattcag gatcaatgta gaaaaacact ggcatatcta ctcccttgc gggattaagc     240
cttggctt caaaacagaa gcactgtatt ttatgaaat actgtccacc ttcaaattgga     300
acaatattgt atgna                                         315

<210> 413
<211> 554
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(554)
<223> n = A,T,C or G

<400> 413
acaggttca ctattacaaa tatatgatgt taaaactaaca aactcatgac cttcaaagat      60
gtcttcgtcc cacgcacaca catttgtat ttgtgtccat ttgtatattc ctttcttcta    120
taatcttcaa attatatagt tatgcattga gttccctatg catctcaccc atctccttta    180
tctcagcctt ctcatacttt gccattctct tcttctgga aataaccaggc acaacaattc    240
cagcaacaac tgctatcacc acaaccacaa taacagcaat aacaccagct ttttagaccct   300
gcattgagaa ttccagggtgt ttttcatcaa cataataaat taaagtttga ccaggatcca   360
gatccagttg ttccccattt actgtcagggt gccattttct tagaatgaaa caaggattca   420
cctttaacat cttttcaaa ataataagcc acatcagcta tgtccacatc attctgagnt   480
ttttgagaag aattttgaac cagatcaata gtgataacat tattctcata caaaataactc   540
gngataaaatt ntgg                                         554

<210> 414
<211> 267
<212> DNA
<213> Homo sapien

<400> 414
accagaaagg cacacgattt tacaatattt gttggaatta ccttactttt taacctccctc   60
atagcagttt tggttgagt atattgatga aagccaaagt ctggtatcta aaacttgggc   120
caatgttcc caactggat atgtcaggct ttcccaatag cttaactgtg accctatacg   180
gatggcttt tagatagttc tatactgctg tattgtgtta gcactttct ttgtcattaa   240
caacacactt taaatgacat ttgggtga                                         267

<210> 415
<211> 454
<212> DNA
<213> Homo sapien

```

<400> 415

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accggaacct gcagaaaacag tgtgagaaat taagtccctgg ttcactgcgc agtagcaaag      60
atggtcaagg ccatggaaaa agcagaaaatt taccaagaaa gctgataccc atgtatagtt     120
cccactcatc tcaaatacat ctgctatctt tttaagctaa gtcctagaca tatcggggat     180
aacatggggg ttgatttagt accacagtt tcagaagcag agaaaatgtaa ttccatattt     240
tatttgaac ttattccata tttaattgg atattgagtg attgggttat caaacaccca     300
caaactttaa ttttgtaaa ttatatggc tttgaaatag aagtataagt tgctaccatt     360
tttgataaac attgaaagat agtattttac catcttaat catcttgaa aatacaagtc     420
ctgtgaacaa ccactcttc acctagcagt atga                                454
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<210> 416
<211> 370
<212> DNA
<213> Homo sapien

<400> 416

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ccgacacggc gccagcgccc tgctgcgtgc cgcgcagcta caatccccatg gtgctcattc      60
aaaagaccga taccggggtg tcgctccaga cctatgtatgc cttgttagcc aaagactgcc     120
actgcataatg agcagtcctg gtccttccac tgcgtcacctg cgcggaggac gcgcacccatg     180
ttgtcctgcc ctgtggatg ggctcaaggt tcctgagaca cccgattccct gcccacacag     240
ctgtattttat ataagtctgt tatttatttataatttatttgggtgacccctt ctggggact     300
cgggggctgg tctgatggaa ctgtgtatattt atttaaaact ctggtgataa aaataaagct     360
gtctgaactg                                370
```

<210> 417
<211> 463
<212> DNA
<213> Homo sapien

<400> 417

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acactttata tattccaaat tgcatacata tatggtttgc aaattcatct caatctgtatg      60
cttatctttt ccttttctta aatcacaatgt tttaaaatattt tgaagaagtc caatatatca     120
gattttgtct ttatggatg tgcttcggg gcaaaagtccca agaacttgc acctagccca     180
agatcctgaa gattttctc ctgtggcttt ttcaaaatgtt atctatgtttt atgtatcaca     240
tttaagtccy ttatcacattt tgagttaaat ttatataag atgtgagggtt taatgttagagg     300
ttcttttttc tcctcgccat ggggtctaa ttgctctagc ataatttgc agaaaggcta     360
ttcttcctcc attgaattgc tttttcaattt ttcaaaatc agctgagcat atttatatgg     420
gtttattttctt gggttctctc atctgttcca ttgacgtatgt tgt                                463
```

<210> 418
<211> 334
<212> DNA
<213> Homo sapien

<400> 418

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ttagcatttt cttttatattt ttactttga tgcctttca aattggcatg tctttaaatgt      60
atttttcttc ctgattaaaa atgtgtgtgt atgtgtgtgt gtgtgtgtat atatatattt     120
tttaaatca cattaattttt accaagtgaa accaagccat actgttttttgc agccaaattaa     180
aaaaattgcc atttttaaag tgcgttttttgc cagggtaaag accccatgaaa tggcttgatg     240
tattcttagac tactgaaaga aaaccacttc aaagatttttgc ttgaaatgttt tagtgttgc     300
tgaaatgcaa gagggaaaggt gattggtagt gagt                                334
```

<210> 419
<211> 297
<212> DNA

<213> Homo sapien

<400> 419

acttcttgta ccaaggaata ccacagacac cctaccgata gaacagtggc tcagatctta	60
cttgctcctg cttacgaagt attcccaatc actggtcatt tgaccctact tgaacactcc	120
tgaacagtca tgtttttaa aatcttcctt tatatcaagt cagagagtat acttctataa	180
atttcactca tggatgttag gaaatctagt catctccct gtgattgccccc tgttaagtat	240
ttaaccatag ctatcatgtg tttcccaaattt cttctctaga ttaaatatct tcagtt	297

<210> 420

<211> 418

<212> DNA

<213> Homo sapien

<400> 420

acgagaggaa ccgcagggttc agacattgg tttatgtcct atcaatagga gctgtatgg	60
ccatcatagg aggcttcatt cactgatttc ccctattctc aggctacacc ctagaccaaa	120
cctacgc当地 aatccatatttgc gctatcatat tcatcgccgt aaatctaact ttcttccac	180
aacactttctt cggcttatcc ggaatcccc gacgttactc ggactacccc gatacataca	240
ccacatgaaa tatectatca tctgttaggtt catttcatttc tctaacagca gtaatattaa	300
taattttcat gatttgagaa gccttcgtt cgaagcgaaa agtcctaata gttagaagaac	360
cctccataaaa cctggagtga ctatatggat gcggccacc ctaccacaca ttgcgaaga	418

<210> 421

<211> 304

<212> DNA

<213> Homo sapien

<400> 421

acgcctggac ccctgtgact tgcagccat ctttgatgac atgctccact ttctaaatcc	60
tgaggagctg cgggtgattt aagagattcc ccaggctgag gacaaacttag accggctatt	120
cgaaattattt ggagtcaaga gccaggaagc cagccagacc ctctggact ctgtttatag	180
ccatcttcctt gacctgctgt agaacatagg gatactgcat tctggaaattt actcaatttt	240
gtggcagggtt gttttttaa ttttcttctt tttctgattt ttgttgttttgggtgtgtt	300
gtgt	304

<210> 422

<211> 578

<212> DNA

<213> Homo sapien

<400> 422

actgtgcagg cagattcaca gggtggtggtaa aagcatcca caatggctct ggcagcatca	60
ggatcacact tgaaggggct ctcagacaaa gttgtattca tgcaactgat tcctttcca	120
ttcgtttctt tagtcaacta tgcttccaa tggcatgat tgcttttaat aatatcaatg	180
gcaaaatctt tatctttaaa ttctgcatta aacgcaaactt cattttctgg tttccatca	240
ggaaccttat accttctaaa ccagtcaca gtagcttcta agtagccagg tttcagccgt	300
ttgacatcat ttagatcatataatggct gcatcaggat catccacatt aatggcaatg	360
actttccatgtt cgtttcccc ttctgtatc atagccaata tgccttagaac tttcaatttt	420
ttatccatcc tcttgcacat accttgcttc caatttcaca cacatcaattt gggtcattgt	480
caccacaaca gccagttatgtt ttagtattgtt gcccgggtt tcccaagtc tgagggatgg	540
caccatagttt ccatatacg ggaacaaa	578

<210> 423

<211> 327

<212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(327)
 <223> n = A,T,C or G

<400> 423

acagtatatt tttagaaaact cattttctta ctaaaacaaa cacagttac ttttagagaga	60
ctgcaataga atcaaaattt gaaactgaaa tccttgcctt aaagggttaa gttgaggcaa	120
gaggaaagcc ctctctctct cttataaaaa ggcacaacct cattggggag ctaagctagg	180
tcattgtcat ggtgaagaag agaagcatcg ttttatatt taggaaattt taaaagatga	240
tgyaaagcac atttagcttg gtctgaggca gttctgttg gggcagtgtt aatggaaagg	300
gctcaactgnt gntactacta gaaaaat	327

<210> 424
 <211> 384
 <212> DNA
 <213> Homo sapien

<400> 424

acgaaaaata aatccctta aaaactaaat aaaatgcact gtattctac agttaatgtt	60
tataactata gtaaaaaatt aatatatatc ctattacata aatgttattt cttaggttt	120
ccattaagaa gagcaataga ataatgctaa aaaataatgc ctataaatct tcagatata	180
aagacatcca ttcagaaaca aaaattagca ctaaattttt tataaaatag accagatgac	240
aaaatttatt ttatTTTaa acagtggtt tgacacaaat tatgttattt aaaaagcatta	300
ttaatgttta atttatttaa aattttggaa ttgcattt ctcagagaat gatcaggcct	360
taggaaatta atacagttagt agta	384

<210> 425
 <211> 255
 <212> DNA
 <213> Homo sapien

<400> 425

actatcaggc ttgtgctga ttccctgaac aaactgcatt atattatgaa aacaaaagga	60
aaagaagaaa taataaaaac tatactccc tatttcactt acagtgttg agttcctgaa	120
aggacctata taatggaggc agcattcaaa caagaaatta tgccaatcaa ctgtcaaatt	180
ttcactataa ttccctaaa aaggcgTTT tcccccaata tctattaatc tcaaagaaac	240
ataagttgtg aatgt	255

<210> 426
 <211> 196
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(196)
 <223> n = A,T,C or G

<400> 426

acatgaantn nccaggccca cacagccaga cagcaacaga accaagacct agggctcttc	60
actcctgtta catcacacca tggcaatgtat ttacattct ccaactgatt caaatcatat	120

ggcagctagg gatttggggg ctccatgtt tatttcaatt gcaagttcaa gatttcttt 180
 tatctttgtg ggctga 196

<210> 427
 <211> 163
 <212> DNA
 <213> Homo sapien

<400> 427
 acagaagatc catggaggca agtgctgtca ggaaggacac tgcctccctc caccctccca 60
 aatgtcacca ccaagttcct tcaggtgaga cctcacacaa tgtcaagtgc tttcttagaa 120
 atactaagat caggttgaga gattctgctt ggtctagtc atc 163

<210> 428
 <211> 315
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(315)
 <223> n = A,T,C or G

<400> 428
 nactgagtagt agatgctggg gaatgtgcaa tatgccttga agaattgcag cagggagata 60
 ctatagcacg actgccttgt ctatgcataat atcataaaagg ctgcatacatat gaatggtttg 120
 aagtaaatag atcttgcctt gagcacccctt cagattaagc gtcaagcttcc tgttttatag 180
 gttttcttgtt cttgacaaga tgcttgaaaa accaagagga tatgaaaatc tgtctctgga 240
 gaaacaaaaga cgcaaggata ctcagccaga aatctgagtt ttgtgagact tggtaataca 300
 gagatggaca atcgt 315

<210> 429
 <211> 131
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(131)
 <223> n = A,T,C or G

<400> 429
 acagtttaggn actagaacat ttgttaagcc tcccaaagta gngtgcattgg aagattctag 60
 agtgcacgc tcttgcacta caaatgtaat aataacagaa taaatacact taccctgatg 120
 atattgaggg t 131

<210> 430
 <211> 503
 <212> DNA
 <213> Homo sapien

<400> 430
 actgattttt aataaaagaa ataaggttca aagtttagca caacaacaca gcaataagaa 60
 gctgacaact tggataaaaa tacaagaaag taacacagag cccaggctac ccattattta 120
 ctgtgtgcac acaggaatgc tataacttcag atgtataaat tagagactga ttttaagttt 180

ttaatttaac tacttttgc ccactgtgct aaactaaatt ttataactaat gtgctactgc	240
gtaaaacactt caaagcaatc ttcattaaaa tgctgcaaag aaaaacaaga atacacatca	300
tccaaaacta aggatgtcat tgcagttcac agtttgtata ataaaataccc tcccttcaa	360
tcactactaa gatcactaca tcctatctac tcatacgac aaccttgaag caacttatac	420
ttacaaatat tagcaatgca gccaaacatt tgttttgc aaagcaacta gtaaaaaatca	480
agaattttaa ttaagacggt gca	503
<210> 431	
<211> 207	
<212> DNA	
<213> Homo sapien	
<400> 431	
acaagtgtgg cctcatcaag ccctgccccag ccaactactt tgcgtttaaa atctgcagtg	60
ggccgccaa cgtcgtggc cctactatgt gcttgaaga ccgcatagtac atgagtcctg	120
tgaaaaacaa tgtggcaga ggcctaaaca tcgcccgtt gaatggaacc acgggagctg	180
tgctggaca gaaggcattt gacatgt	207
<210> 432	
<211> 485	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(485)	
<223> n = A,T,C or G	
<400> 432	
aaaaaaaaatgaaaaat ggttgcaggt ttaatcncaa aangaactta attttngtng	60
attttgtttt atctgctaaa acactaatat ctataaaatat gaactgacag catcgttcta	120
aatttacttc tgaagagctg tcgagacttc aataaaaatat aagcaagttt ctggatcata	180
tttatggact gctgaattaa ctacccaaaa agtatacgat actttcaaag aacacaaaaac	240
aaagtgaacg tggaaaaaaag ctttcttgc aaaagtccctt ttatttagtcc tattctctaa	300
aattccaagc cacagagcct tggatattcct ggattctgtt ttaagtaacc ttagtttaa	360
atatgacact tggatatgc acaatggaa aggttaggat atgtgaacaa aatttaattt	420
ctttttcca aagnagnca ttttctttaa atncatccta tccacttttgc cccacttccc	480
catgt	485
<210> 433	
<211> 280	
<212> DNA	
<213> Homo sapien	
<400> 433	
actgtcacta caatattaca ttctgcaaatt gtattctgt tgtatcagat aaaaaatttt	60
agtggaggat ctctaaggca catagtagaa aacaaaattt gtttattactt caagttccctt	120
tcactgtgtat ttggaaatga tttaatctttt atagaatgag aacctttttt ggactagctt	180
ttttattaaaa atggctcaat ttgtgtgtat aaggattgca ttatattta atagtgcgtt	240
cttttcctct gggcacacca ttttgatcat taaccagagt	280
<210> 434	
<211> 234	
<212> DNA	
<213> Homo sapien	

gtggagcaca ggaaggaaat ggctgggtgg tcagagagag gtgagctgtc ggagaaacac	240
agttaaacta aaaaataaaa tccattttgt gtataaactg acttaaacgc atgcaaagaa	300
gtggaaaaca tatgccattt gtcaagaaaa atactgcttt atagcttttta ctttacaatt	360
aaaggagaaa gcagaggcca gatataagcc cagataataa catttaagtt ttcataaaaa	420
ctcccaaatg t	431
<210> 439	
<211> 170	
<212> DNA	
<213> Homo sapien	
<400> 439	
actgtcataa aaaacagtgg agctctgtat tagaaagccc ctcagaactg ggaaggccag	60
gttaactctag ttacacagaa actgtgacta aagtctatga aactgattac aacagactgt	120
aagaatcaaa gtcaactgac atctatgcta catattatta tatagtttgt	170
<210> 440	
<211> 400	
<212> DNA	
<213> Homo sapien	
<400> 440	
acgtaaaaag aacatccttc ccatcttcaa ggtcaagatt gaacgctgac tcctgcagga	60
agtcttccag gatcccagg caggaatgtat ggctccctgt ccctgttagct ccaggagttc	120
ttgcttcacg cacgcctcac ataccagact gaatgttgc aggaggagtg accaggtcg	180
tcatctgtgt ccctaccacc tacaacaggc cagcaatcta cccgtgtgt tttgttggac	240
agaattaacc atgatggcg gccgagggcg cctggagcta tttggggct tggagagaac	300
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<213> Homo sapien	
<400> 441	
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aagcactgtct gtgaaatgtg aagt	204
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<400> 442	
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catggtattt atgagtctcc aaactattgg aaatttattt caaccaaggt tctcttaagt	180
tttcattact tgggtgtaac tcgagagaaa actaatttat atcaatttac agtttagtgg	240
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gaactttcc tttattccta atatacagga caaaccttgc cgacatctca ctacctaaa	360
aatcaaattt aaatgaagta tccaggagta gcctaaagaa tgagtgtaat ctggatggat	420
tttagtctaa atttagcct tgctcttcag taaagtatag taactccaga tatatgttcc	480

acagatgcaa taatttctgt tccttggcgtgcagaata taatttatac ttcctgaaat	540
caactttgtc tattcatgaa aatagctgct ttttatttgc ctttgcctca ctttgaatat	600
atatgatcca caggttacag actttccaa taactacatt tcaacttgt	649
<210> 443	
<211> 346	
<212> DNA	
<213> Homo sapien	
<400> 443	
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acttttgtca taacctcago attgtcagat aacctcagt agttaactca aagccttta	120
ttatggaaaag aactggcaca gttacatttg ccagtggcaa catcctaaa attaataac	180
tgtatgggtca cggacagatt tttgacctag ttcccttttc ttttagagca aaaagaactt	240
ttacctcggc atccagccca acccctaaag actgacaata tccttcaagc tcctttgaaa	300
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<211> 425	
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<213> Homo sapien	
<400> 444	
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tgtgctgccg tccacaagca atctcagtga caatgttcc cataagttca aaaactttcc	180
ttggggttat ttcatgactg gtatgtttttt ggccttactg accataccct ccagctccaa	240
aagtaaacac tccaccttcc ttgggttagag cagcgtatg atcttctcca caacaatata	300
aaactatttt ctgagatctt agtgcatttta gtaaattagg aacataaccta tcattttcat	360
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tgagt	425
<210> 445	
<211> 210	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(210)	
<223> n = A,T,C or G	
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taaactggca gcagggttag acattactttt caaagcttga ggttagaccga gtcagcatgc	180
tagacaggct tctctctcta accaaaactg	210
<210> 446	
<211> 326	
<212> DNA	
<213> Homo sapien	
<400> 446	
tcgaaagacc cctgtaaaag agcccaacag tgaaaatgtt gatatcagca gtggaggagg	60

cgtagacaggc tggaaagagca aatgctgctg agcattctcc tgttccatca gttgccatcc	120
actaccggc ttcttcttct tgctgaaaaa taaaccactc tgcccatttt taactctaaa	180
cagatatttt tgtttctcat cttaactatc caagccaccc attttatttg ttctttcatc	240
tgtgactgct tgctgacttt atcataattt tcttcaaaca aaaaaatgta tagaaaaatc	300
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<210> 447	
<211> 304	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
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<223> n = A,T,C or G	
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cttggtggtt gagtccattc tgcccaagtg gttttcaag caggagagtg cccactgtcc	240
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<210> 448	
<211> 203	
<212> DNA	
<213> Homo sapien	
<400> 448	
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agcgcatttt cattagttgg acaaacaacc ttataaacc ttatgtcaaa ccatataatg	120
tgaagaatct ccatgggaga gatTTTTT cacccttcag aattatcttt ttcccctaag	180
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<210> 449	
<211> 481	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1)...(481)	
<223> n = A,T,C or G	
<400> 449	
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aaagctttttt agtgatcatt tattacttg tgtttacttag atattaattc taagatgaat	180
tccttttagaa ttttagaaaaa aattatctta gacaacaatc aaagtaaagg atacatccag	240
cattgaaacc ataagccggc aagtctccag gttaaaaggt ttgtatcctc cagcaatgcc	300
agactgtgtc agacatctct gcaattcattc agcatctatc tgcccatctc gtccagctac	360
agcagcaaaag taaccataca gcggatcctg agtttgcgttccg ggaaacgcag gccctccggg	420
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g	481

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<210> 450
<211> 296
<212> DNA
<213> Homo sapien

<400> 450
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aaacactcaa aacatttcc attggaaaca tggaaagaca atatgaggtt ttgttaccat     120
cttactgcaa ttttcttatg tgtagtact ctacataccc catgtttct gtaatcatgc     180
agatgtaat ggaagttga atgattaaat aaatgaaaag tccgttact gcagggaaatc    240
atttcacaag gcagccaaac cgggtttaga gaacaaaact attcaagaaa ttctcc     296

<210> 451
<211> 294
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(294)
<223> n = A,T,C or G

<400> 451
acatgntcca aggcacgcgn ctgtgaacct cctctgagtg aaggcatccc ctccagcacc      60
tttcagctg ctatgttagga cgaccgcgg ccaccctcca ggacctccag ccctgcactg     120
ccttcctct ctttaaata attcttcatt gagttctaat atgtaaaaaaaaaa aaagttact     180
gtaaagtttgc caaataanga aattttttt aaaagtccctc agtaatctt ccagtaacaa    240
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<210> 452
<211> 129
<212> DNA
<213> Homo sapien

<400> 452
acttttagat cacaatatttgc ctttaagta acacataata cactaaggc agatggcct      60
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atagaagag      129

<210> 453
<211> 151
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(151)
<223> n = A,T,C or G

<400> 453
actctcaann tgtatggg tgccaaacaca tttaggatca ttgnnnnttc tcagtgaatt      60
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ttataactaa gtcacacttgc tgtggattt t      151

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<210> 454
<211> 119
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(119)
<223> n = A,T,C or G

<400> 454
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agcttgtgtg ttctttgtt aatgtgtaga gttctccctt ctcgaaattt ccagtgtgt      119

<210> 455
<211> 515
<212> DNA
<213> Homo sapien

<400> 455
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tcatgttgtg ccttcttgag tttggccctt aaactgtcta attcggttcc ttttcaatt      120
gctttatgtg ttactgacac aatatcttcc tcaagctgat gggctttgga tgttagcatca      180
ctgaacctt tcttaaactc ttcatcttcc attttaagc tttgtgttac ttcaagtaaga      240
ccctttgtt ctgcttgcag ttggtcacat ctttcttctt catggtaag ttctcttcc      300
attctcccaa cttgttctcg aagttgtgct gtttctttt ccagaacggc aattaacttt      360
aacagttctt cttttcttt catggtttcc tcaatttca actcaagaag gcctgcttt      420
gtggtcacca ctaacatgtc agaatttccct tcatcttcca tagtaagcag ctcttcaact      480
ggagaagaag ctcgaaactg gaaagggtgtc cctgc      515

<210> 456
<211> 350
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(350)
<223> n = A,T,C or G

<400> 456
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acagtggctc agcctacaga gttccctata gggaaaagaa ggcagggaaat aggccgcagg      180
tctggcctg tccctgcacc accctgagca gctagtctt ggaagggatt acaggccctg      240
ggccataggc tgctcgccat tctgcttcc tatcctgttt ctctccctgt gctgctccct      300
tttagccagn gctgagaaat gttcancacc tgaggcaaaa ctgccatagt      350

<210> 457
<211> 293
<212> DNA
<213> Homo sapien

<400> 457
gcagggccaa cagtcacagc agccctgacc agagcattcc tggagctcaa gctcctctac      60

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aaagagggtgg acagagaaga cagcagagac catgggaccc ccctcagccc ctccctgcag	120
attgcatgtc cccttggagg aggttcgtct cacagcctca cttctaacct tctggAACCC	180
accaccact gccaagctca ctattgaatc caccgcattc aatgtcgag aggggaagga	240
ggttcttcta ctgcggcaca acctgccccca gaatcgtatt ggtaacagct ggt	293
<210> 458	
<211> 500	
<212> DNA	
<213> Homo sapien	
<400> 458	
actagactcc agattaccct ttcttaataa atatctcagg gtaaggaaag aaagaaaactg	60
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acaactgcag agttgaatag atgcagcaga tcctttacag aaaaagttt ctgacctcaa	360
ttcttaagta attgttagtag ggagctggag gactttttt ccctttatgg taatTTTTG	420
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atatatttagg aaaataaaaaa	500
<210> 459	
<211> 394	
<212> DNA	
<213> Homo sapien	
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taaggTggcg tgTTgcagtg cagagtgcTT ggctgtttcc tgTTTctcc cgattgcTcc	180
tgtgtaaaga tgcTTgtcg tgcagaaaca aatggctgtc cagTTtatta aaatgcctga	240
caactgcact tccagtcacc cgggcTTgc atataaataa cggagcatac agtgagcacA	300
tctagctgat gataaataca ctttttttcc cttttcccc ctaaaaatgg taaatctgat	360
catacttaca tgtatgaact taacatggaa aatg	394
<210> 460	
<211> 279	
<212> DNA	
<213> Homo sapien	
<220>	
<221> misc_feature	
<222> (1) ... (279)	
<223> n = A,T,C or G	
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tttcaccgct acacgaccgg gggatacta cggtaatgc tctgaaatct gtggagcaaa	180
ccacagtttc atgcccatacg tcctagaatt aattccctta aaaaatTTG aaataggGCC	240
cgtatttacc ctatagcacc ccctctagag caaaaaaaaaa	279
<210> 461	
<211> 278	
<212> DNA	

<213> Homo sapien

<400> 461

tttggacact aggaaaaaac cttgttagaga gagtaaaaaaa tttAACACCC atagtaggcc	60
taaaAGCAGC cACCAATTAA gAAAGCGTTC aAGCTCAACA CCCACTACCT AAAAATCCC	120
aaACATAATAA CTGAACCTCT cacACCCAT tGGACCAATC TATCACCCCTA TAGAAGAACT	180
aatGTTAGTA tAAAGTAACA TGAAAACATT CTCCCTCGCA TAAGCCTGCG TCAGATTAAA	240
acACTGGACT GACAATTAAAC AGCCAATATC TACAATCA	278

<210> 462

<211> 556

<212> DNA

<213> Homo sapiens

<400> 462

aacgtccaag gggccacat cgatgatggg caggcggag gtcttgtgg tttgtattc	60
aatcaCTGTC ttGCCCCAGG ctccgggtgt actcgtgcag ccATCGACAG tgacgctgta	120
ggtgaAGGGG ctgttgccct cggcgcggat ct.cgtatctcg ttggagccct ggaggagcag	180
ggcCTTCTTG aggttgcag tctgctgtc catgtaggcc acgctgttct tgcagtggta	240
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atcggcaggg tcggagccct ggccgcata ctgcgaactgg aatccatcggt tcatgctctc	360
gccgaACCCG acatgcctct tgccttggg gttcttgctg atgtaccagt tcttctggc	420
cacactgggc tgagtgggtt acacgcaggc ttcaccagtc tccatgttgc agaagacttt	480
gatggcatcc aggttgcagc ctgggttggg gtcaatccag tactctccac tcttccagtc	540
agagtggcac atcttg	556

<210> 463

<211> 659

<212> DNA

<213> Homo sapiens

<400> 463

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agtgcacgga agtcacaact ggtctatcag tccagacggg ggcTTTGGT caaatattct	180
tctgattact tccaAGCCCC ctctgactac agatactacc cctaccagtc ctTCCAGACT	240
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cccaccatcc agagctgctg gaactacggc ttctcctgt cctcggacga gctccCTGTC	360
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atgctctgcg aagggtcttt cgtggcagac gtcaccgatt tcgagggtgt gaaggctgcf	480
attcccAGTG ccctggacac caacagctcg aagagcacct cctcCTTCCC ctgcccggca	540
gggcacttca acggcttccg cacggtcata cgcCcCTTCT acctgaccaa ctccTcaggt	600
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<210> 464

<211> 695

<212> DNA

<213> Homo sapiens

<400> 464

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tcaAGGAAT GCCAGCTGCA catcaaggac atcttcagga agttcaggat tgccgtAGCT	180
aaACTGAAAAA CCACCATCCA tggactCTCC aaACCAAACG tGTTTCTCT cAGCAGTAGA	240
atctgtccac cAGTGTTCCTC GTGGAACATT CAAAGGATTG GCACttATGC atGTTTCCCC	300

agtttccata ttacagaata ccttgatagc atccaatttg catccttgg tagggtcaac 360
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ggggttttta cgagaaccat caggactaat gaggtttct atttgtccat taacagactt 480
gagtgaagtc ataatctcat cggtgttgc tttgaaatcc attggttcat ctccataata 540
cgggggcaaaa ccgcacgctt tttcacctcc aatcccagca atggcagcgg ctccaaacacc 600
accacagcaa ggaccagggg caccaggagg tccaggaggg cctgggttgcc ctgggtggcc 660
tggggagccc tcagatcctc tttcacctct gttac 695

<210> 465

<211> 73

<212> DNA

<213> Homo sapiens

<400> 465

caggtccaga gctcccaggt ttccagggtt cagtcctcc agtcccagag ctcccaggg 60
ttcggtttcc agt 73

<210> 466

<211> 507

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(507)

<223> n = A,T,C or G

<400> 466

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aagcatattg ctataacaaga cttaaaagac ttcataaaag ccaaacttgc agagtccttg 120
catggagtag ccaaggaaag tcggagccca tccttagcc aaaccacgaa caccatcctc 180
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cacggcgccg gctgccaggt tgcgagggcg gcggggctgg cccgtggcc ctggggagct 420
gctgcggagg tccccgagac catcgtgcac canctgcaga tgtggcgtgt tgaagggggt 480
cgcccgcgcc aggtgcgcaca cggacga 507

<210> 467

<211> 183

<212> DNA

<213> Homo sapiens

<400> 467

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cttctgagga gcaggaggga gccaccctcc ctgcagctac cctagcttag gaggctgttg 120
tgaggggcag aatgagaaag gcaataaagg gagaaagaaa aaaaaaaaaa aaaaggccgg 180
ccg 183

<210> 468

<211> 129

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature
<222> (1)...(129)
<223> n = A,T,C or G

<400> 468
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acnccaang 129

<210> 469
<211> 243
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(243)
<223> n = A,T,C or G

<400> 469
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ggggcagtgg ccatggaggc cgtgctgaac gagctgggtgt ctgtggagga cctgctgaag 120
tttggaaaaga aatttcagtc tgagaaggca gcaggctcg tgcacaagag cacgcagttt 180
gagtaacgcct ggtgcctgtt gcggagcaag tacaatgtat acatccgtaa aggcatcg 240
ctg 243

<210> 470
<211> 452
<212> DNA
<213> Homo sapiens

<400> 470
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gcagtgcgtc tgtctcgaaaa gggttttcat ctatgagggt gtttcctcta aacctacgag 420
ggaggaacac ctgatcttac agaaaatacc ac 452

<210> 471
<211> 168
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(168)
<223> n = A,T,C or G

<400> 471
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taccatgtcc atcagggtga cccagaagtc ctacaagggtg tccacccttg gccccccggc 120
cttcagcgc cgtcctaca cgagtgggcc cggttccgc atcagctc 168

<210> 472

<211> 479

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(479)

<223> n = A,T,C or G

<400> 472

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tggagcctca ncagtccct ctttcanaac tcactgcca gaggcctgaa caggagccac 120
catgcagtgc ttcaagaccat gatgatcctc ttcaatttgc tcatctttct 180
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<213> Homo sapiens

<400> 486

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(54) Title: COMPOUNDS FOR IMMUNOTHERAPY AND DIAGNOSIS OF COLON CANCER AND METHODS FOR THEIR
USE

(57) Abstract: Compositions and methods for the therapy and diagnosis of cancer, such as colon cancer, are disclosed. Compositions may comprise one or more colon tumor proteins, immunogenic portions thereof, or polynucleotides that encode such portions. Alternatively, a therapeutic composition may comprise an antigen presenting cell that expresses a colon tumor protein, or a T cell that is specific for cells expressing such a protein. Such compositions may be used, for example, for the prevention and treatment of diseases such as colon cancer. Diagnostic methods based on detecting a colon tumor protein, or mRNA encoding such a protein, in a sample are also provided.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/30909

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7	C12N15/12	C07K14/47	C12N5/10	C07K16/18	C12N15/62
	C12Q1/68	G01N33/50	G01N33/53	A61K38/02	A61K48/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K C12N C12Q G01N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LIU,W.L., ET AL.: "identification and characterization of novel full-length cDNAs differentially expressed in human hematopoietic lineages" EMBL SEQUENCE DATA LIBRARY, 12 November 1998 (1998-11-12), XP002137433 heidelberg, germany accession no. AF097021 ADAMS, M.D., ET AL.: "initial assessment of human gene diversity and expression patterns based upon 83 Million Basepairs of cDNA sequence" EMBL SEQUENCE DATA LIBRARY, 18 April 1997 (1997-04-18), XP002137434 heidelberg, germany accession no. AA366895 -/-/	1,2,4-8
X		1,2,4-8

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

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PCT/US 99/30909

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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A	WO 98 53319 A (KINZLER KENNETH W ;VOGELSTEIN BERT (US); UNIV JOHNS HOPKINS (US)) 26 November 1998 (1998-11-26) the whole document ---	
A	J-M FRIGERIO ET AL: "Analysis of 2166 clones from a human colorectal cancer cDNA library by partial sequencing" HUMAN MOLECULAR GENETICS,GB,OXFORD UNIVERSITY PRESS, SURREY, vol. 4, no. 1, 1995, pages 37-43-43, XP002111970 ISSN: 0964-6906 ---	
A	GRIMM T ET AL: "A modified screening method for pcDNA-1 expression libraries which is applicable to both surface and intracellular antigens Cloning of a colon carcinoma antigen" JOURNAL OF IMMUNOLOGICAL METHODS,NL,ELSEVIER SCIENCE PUBLISHERS B.V.,AMSTERDAM, vol. 186, no. 2, 16 October 1995 (1995-10-16), pages 305-312, XP004021231 ISSN: 0022-1759 ---	
A	YEATMAN, T.J. AND MAO,W.: "identification of a differentially-expressed message associated with colon cancer liver metastasis using an improved method of differential display" NUCLEIC ACIDS RESEARCH,GB,OXFORD UNIVERSITY PRESS, SURREY, vol. 23, no. 19, 1995, pages 4007-4008-8, XP002099962 ISSN: 0305-1048 the whole document ---	
A	CHAN ERR-CHENG ET AL: "Identification of novel genes that are differentially expressed in human colorectal carcinoma." BIOCHIMICA ET BIOPHYSICA ACTA SEPT. 30, 1998, vol. 1407, no. 3, pages 200-204, XP000910494 ISSN: 0006-3002 figure 2 ---	
		-/-